#24

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Application of Delovitch, T. L.	)	Examiner: J. H. Roark
Serial No.: 09/341,407	)	Group Art Unit: 1644
Filed: October 12, 1999	)	
For: METHODS AND COMPOSITIONS FOR PREVENTING AUTOIMMUNE DISEASE	)	

Date: February 26, 2003

DECLARATION OF TERRY L. DELOVITCH

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

I, Terry L. Delovitch, do hereby declare and say as follows:

1. I am presently Director and Scientist, Autoimmune Diabetes Group, John P. Robarts Research Institute, London, Ontario, Canada. I am also Professor, Department of Microbiology and Immunology, at the University of Western Ontario. A copy of my curriculum vitae is attached as Exhibit 1 to this Declaration.

2. I am the inventor named in the above-identified application and have read and understood the Office Action mailed on August 27, 2002.

3. The Examiner has rejected claims 1 to 6 and 8 to 9 under 35 U.S.C. 103(a) as unpatentable over Rabinovitch (Diabetes (194), v. 43, pp. 613-621)

and Lenschow et al. (Immunity (1996), v. 5, pp. 285-293) in view of either King et al. (Eur. J. Immunol., (1995), v. 25, pp. 587-595) or Webb et al. (Blood (1995), v. 86, pp. 3479-3486).

4. Rabinovitch (1994) discusses findings that both non-specific (e.g. using viral and bacterial materials) and specific stimulation of the immune system were able to reduce or prevent development of IDDM in NOD mice. They speculate that these interventions are effective by down-regulating Th1 T cells and up-regulating Th2 cells.

5. Subsequent to publication of the Rabinovitch paper, but before the priority date of the subject application, continuing studies of immune stimulation to prevent autoimmune diabetes gave results inconsistent with Rabinovitch's findings and revealed that predictions from Rabinovitch's findings did not hold true. For example, several clinical trials were conducted in humans using administration of the Bacillus Calmette-Guerin (BCG) vaccine to prevent development of diabetes, but this approach to using immune stimulation failed to prevent development of diabetes - see, for example, Dahlquist et al., (1995), Diabetologia, v. 38, pp. 873-874 (copy enclosed).

6. I believe that in view of these conflicting findings, one of skill in the art at the relevant time would not have had a reasonable expectation of success in treating or preventing IDDM by immunostimulation or by up-regulating the Th2 arm of the immune response.

7. The Lenschow reference presents a very confusing picture of the role of the CD28 pathway in the development of IDDM in NOD mice. The authors found that disruption of the CD28 pathway at 0 to 2 weeks of age gave an increased prevalence of IDDM in NOD mice, whereas disruption at 2 to 5 weeks had no effect on disease incidence and disruption at 5 to 7 weeks gave suppression of the disease (page 290, column 2).

8. The authors also observed that CD28-negative NOD mice had T cells which responded poorly to many antigens but maintained a strong response to the IDDM-associated autoantigen, GAD. They note that "these results suggest that GAD-specific T cells can develop in the absence of CD28 co-stimulation."

9. In trying to explain the occurrence of GAD-sensitive T cells in CD28-negative mice, the authors also note that other co-stimulatory molecules which are present in these mice may substitute for CD28 in these mice (page 289, column 2).

10. Those of ordinary skill in the art were aware at the relevant time of alternative co-stimulating mechanisms such as CD43 (Sperling et al., (1995), J. Exp. Med., v. 182, pp. 139-146), CD40L (Greval et al., (1996), Science, v. 273, pp. 1864-1867), and LFA-1 (Wingrein et al., (1995), Crit. Rev. Immunol., v. 15, pp. 235-253). One of skill in the art would have been aware that these co-stimulating pathways were present and active in the CD28-negative NOD mice described in Lenschow's studies.

11. The Examiner concludes that, based on Lenschow's showing that inhibition of CD28 signalling during the first two weeks of life exacerbates IDDM, this would "suggest to one of ordinary skill in the art at the time of the invention was made that the opposite method of stimulating CD28 signalling during this critical window would have the opposite effect of inducing a TH2 response and protecting from development of diabetes."

12. I do not believe that one of skill in the art at that time would have drawn that conclusion regarding the effect of stimulating CD28 signalling in view of the likelihood that other co-stimulatory molecules were compensating for lack of CD28 in these animals, as noted by Lenschow at al., and in view of the fact that

the critical autoantigen-sensitive T cells were able to develop normally in the absence of CD28 signalling.

13. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardise the validity of the application or any patent issued thereon.

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Terry L. Delovitch Date:

November, 2002

CURRICULUM VITAE

Terry Leonard Delovitch

PERSONAL DATA

Birth Date/Place December 17, 1945; Montreal, Quebec (Canada)

Nationality Canadian

Status Married, wife - Regina
2 daughters - ages 30 and 27.

Address
Autoimmunity/Diabetes Group
The John P. Robarts Research Institute
1400 Western Road
London, Ontario N6G 2V4, Canada
Tel: (519) 663-3972
Fax: (519) 663-3847

EDUCATION

Degrees	B.Sc. (Honors Chemistry) McGill University	1966
	Ph.D. (Department of Chemistry) McGill University	1971
Graduate Student	Laboratory of Biophysical- and Immuno- Chemistry Department of Chemistry McGill University (with Dr. A. Sehon)	1966-69
	Department of Immunology University of Manitoba (with Dr. A. Sehon)	1969-71
Postdoctoral Fellow	Department of Biology Massachusetts Institute of Technology (with Dr. Corrado Baglioni)	1971-73
	Department of Medicine/Immunology Stanford University (with Dr. Hugh O. McDevitt)	1973-75

APPOINTMENTS

Assistant Professor	Banting and Best Department of Medical Research University of Toronto	1976-80
Associate Professor	Banting and Best Department of Medical Research University of Toronto	1980-84
Professor	Banting and Best Department of Medical Research University of Toronto	1984-93
	Department of Immunology University of Toronto	1984-93
	Department of Microbiology & Immunology University of Western Ontario	1994-
	Department of Medicine University of Western Ontario	1997-
	Leave of Absence	2002
	Sabbatical	2003
Visiting Scientist	Centre d'Immunologie de Marseille-Luminy (Sabbatical with Dr. Bertrand R. Jordan)	1982-83
Member	Institute of Immunology University of Toronto	1976-84
	Banting and Best Diabetes Center University of Toronto	1985- 93
Director	Autoimmunity/Diabetes Group The John P. Robarts Institute	1994-
	CIHR/JDRF Diabetes Interdisciplinary Research Program (DIRP)	1995-00
	ORDCF Diabetes Research Centre	2001-
Chief Scientific Officer	Diabetogen Biosciences Inc.	2000-

AWARDS, MEMBERSHIPS, EDITORIAL BOARDS

Awards	National Research Council of Canada Studentship	1966-67
	National Research Council of Canada Postgraduate Scholarship	1967-70
	American Cancer Society Senior Dernham Fellowship in Oncology	1973-75
	Centre Nationale Recherche Medicale Visiting Scientist Fellowship	1982-83
	Fondation pour la Recherche Medicale Visiting Scientist Fellowship	1982-83
	Sheldon H. Weinstein Scientist in Diabetes (Endowed position)	1994-
	Medical Research Council-University Industry Program Development Grant in Diabetes (Director, Autoimmunity/Diabetes Group)	1994-99
	Medical Research Council of Canada/ Juvenile Diabetes Foundation International Diabetes Interdisciplinary Research Program (Co-Director)	1996-01
	Ontario Research and Development Challenge Fund Diabetes Research Centre (Co-Director)	2000-05
Memberships	Canadian Society for Immunology	1971-
	American Association of Immunologists	1976-
	Canadian Diabetes Association	1989-
	Juvenile Diabetes Foundation International	1990-
	American Association for Advancement in Science	1990-
	American Diabetes Association	1994-
	Immunology of Diabetes Society	1995-
Editorial Boards	Immunogenetics	1988-90

Research in Immunology	1991-96
Therapeutic Immunology	1994-98
Journal of Immunology	1994-98
BioMed Central Immunology	2001-

SCHOLARLY, PROFESSIONAL AND ADMINISTRATIVE ACTIVITIES

1. **Journal Manuscript Reviewer**
Science, Immunity, Nature Immunol., Nature Reviews Immunology, J. Exp. Med., J. Clin. Invest., Mol. Cell. Biol., J. Immunol., Proc. Natl. Acad. Sci. USA, Diabetes, Cancer Res., CRC Crit. Rev. Sci., Int. Immunol., Immunol. Today, Cytokine, J. Endocrinology, J. Autoimmunity, Autoimmunity, Res. Immunol., FASEB J., Diabetologia, Therapeutic Immunol., J. Immunol. Methods, Immunology Letters, Immunogenetics, J. Immunogenetics, Scand. J. Immunol.

2. **Granting Agency Member**
Chairman, NCI of Canada Immunology Grants Panel, 1985-86; Canadian Diabetes Association Grants Panel, 1986-90; Honorary Secretary Treasurer and Member, Grant Review Committee, Banting Research Foundation, 1987-89; Chairman, Grant Review Committee, Banting Research Foundation; 1989-90; NIH Immunological Sciences Study Section (Autoimmunity), 1991; Juvenile Diabetes Foundation International (JDFI) Program Grants Panel, 1991; NIDDK/NIH Diabetes Endocrinology Research Centres (DERC) Grants Panel, 1992; Multiple Sclerosis Society of Canada Grant Review Panel, 1993-94; Arthritis Society (Canada), 1998-99; JDRFI Medical Science Review Committee, 1994-2001; CIHR Canada Research Chairs Program College of Reviewers, 2001-present; NIH TrialNet Type 1 Diabetes Study Group, 2001-present.

3. **Granting Agency Site Visit Teams**
MRC of Canada, Dept. of Immunology, University of Alberta, Edmonton, 1985; MRC of Canada, Program on Autoimmunity and Transplantation, McGill University, Montreal, 1986; NCI/NIH Cancer Preclinical Program: - Medical Biology Institute, San Diego, 1986 - Representative from Site Visit Team to NCI/NIH Cancer Preclinical Program Project Parent Review Committee, Bethesda, 1986; NCI/NIH Cancer Program, University of North Carolina, Chapel Hill, NC, 1989; Chairman, MRC of Canada Site Visit Team, Program on Autoimmunity and Transplantation, McGill University, 1989; NCI/NIH Cancer Program, Sloan Kettering Institute for Cancer Research, New York, 1990; Cystic Fibrosis Foundation, RFA for Host-Resistance Program in Cystic Fibrosis, McGill University, 1992; Chairman, NIDDK/NIH Site Visit Team, UCLA Program Project on Type I Diabetes, 1992; Chairman, MRC of Canada Site Visit Team, Development Grant Application in Pharmaceutical Biotechnology: Formulation and Delivery of Protein and Peptide Drugs, University of Alberta, 1993; Chairman, NIH Special Review Panel, Centers of Excellence in Autoimmunity, June 1999; NIDDK/NIH Special Emphasis Review Panel of Diabetes Centers of Excellence, December 1999; JDFI-NHMRC Australia Program Project Review Panel, Walter and Eliza Hall Institute, Melbourne, Australia, February, 2000; Wellcome Trust-JDFI Diabetes and Inflammation Laboratory Project Review Panel, Wellcome Trust, London, U.K., June 2000.; NIDDK/NIH Special Emphasis Review Panel of Diabetes Centers of Excellence, June 2001 and June 2002.

4. **Granting Agency Ad Hoc Reviewer**
MRC/CIHR; Immunology Study Section, NSF (USA); Experimental Immunology Study Section, NIH (USA); Special Study Sections, NIH (USA)/AI and NIDDK; Immunology and Transplantation Grants Panel, Canadian Red Cross Society; NSERC; Canadian Diabetes Association; Hospital for Sick Children Foundation,

Ontario Ministry of Health, B.C. Health Care Research Foundation, Multiple Sclerosis Society, Banting Research Foundation, Washington University Diabetes Research and Training Center, Alberta Heritage Foundation for Medical Research, Arthritis Society (Canada); Human Frontier Science Program.

5. **Host**
Gairdner Foundation awardee, Dr. Peter Doherty, 1986.

6. **Consultant**
Novo-Nordisk, Immunity to Insulin 1986-88; Genentech, Pre-Clinical Trial on Cytokine Therapy of Type I Diabetes, 1993; SmithKline Beecham, 1996; Bioniche Inc., 1996; Member, Scientific Advisory Board, Hemosol Inc./X-Cell Div., 1996-1999.

7. **Administrative Committees**

Member (U. of Toronto, 1976-93): Membership Committee, Institute of Immunology, 1976-83; four Institute of Immunology M.Sc. thesis defence committees, one Institute of Medical Science M.Sc. thesis defence committee, three Institute of Immunology Ph.D. thesis defense committees, one Dept. of Microbiology Ph.D. thesis defence committee, and six Dept. of Immunology, U. of Toronto, M.Sc./Ph.D. thesis defense committees, 1976 -93; Vice-Provost's Working Group Committee to re-design animal facilities of the Banting and Best Institutes, 1978; Search Committee for Chairman of the Banting and Best Department of Medical Research (BBDMR), 1978-79; Executive Committee, Division IV, School of Graduate Studies, 1978-79; twelve Institute of Immunology/Dept. of Immunology student research advisory committees, 1977-93; Medical Faculty Advisory Committee on Animal Services, 1978-86; Medical Faculty Council Assembly, 1978-93; Institute of Immunology Review Committee, 1979-80; C.H. Best Postdoctoral Fellowship Selection Committee, 1983-87; Biochtechnology Search Committee, Depts. of Immunology and Medical Genetics, 1984-85; Executive Committee, Dept. of Immunology, 1984-87; Promotions and Policies Committee, Dept. of Immunology, 1984-93; International Congress of Immunology Symposium Toronto Organization Committee, 1984-85; Immunology of Diabetes Search Committee, BBDMR, 1985-86; Dean of Medicine Committee on Site Review of Banting and Best Diabetes Centre, 1987; Research and Development Committee, Banting and Best Diabetes Centre, 1987-93; Fraud and Ethics in Research Committee, Faculty of Medicine, 1988-91; Personnel Support Committee, BBDMR, 1988-91; Search Committee for Assistant Professor, BBDMR, 1991; C.H. Best Fellowship Committee, BBDMR, 1991-93.

Member: (RRI/UWO, 1994-2000): Robarts Research Institute (RRI) Scientific Advisory Council, 1994-present; RRI Group Directors Advisory Committee 1994-98; J. Allyn Taylor Award RRI Nomination and Selection Committees, 1994-present; RRI Animal Users Committee, 1994-present; RRI Credentials and Promotion Committee, 1994-present; Promotions and Tenure Committee, Faculty of Medicine, UWO, 1997-98; Promotions and Tenure Committee, Ivey School of Business, UWO, 1996-99; Department of Microbiology and Immunology Research Committee, UWO, 1998-present; Scientific Committee, Alan Thicke Centre for Juvenile Diabetes Research; International Scientific Committee, 75th Anniversary Symposium of the

Discovery of Insulin, 1995-96; Faculty of Medicine and Dentistry Dean's Task Force on Research Priorities, 1999-2000.

Chairman (U. of Toronto, 1976-93): two Senate Oral Ph.D. Committees, School of Graduate Studies, 1979-81; C.H. Best Fellowship Committee, BBDMR, 1985-87; Promotions Committee, BBDMR, 1988-91.

Chairman (RRI/UWO, 1994-2000): RRI Group Directors Discussion Group 1995-96; RRI Immunology Search and Selection Committee, 1995-present; RRI Animal Users Committee, 1994-95; Research Committee, Dept. of Microbiology and Immunology, UWO, 1996-98; M.Sc. Student Thesis Defense Committee, Dept. of Microbiology and Immunology, UWO, Sept./96; Diabetes Research Centre Search and Selection Committee, 2000-present.

Chairman (2002- present): Scientific Advisory Board, Diabetogen Biosciences Inc.

Student Advisory Committees

A. University of Toronto - Member of 23 student advisory committees, 1976-93.

B. University of Western Ontario

1. Henry Chou, Dept. of Microbiology and Immunology, UWO, Sept./94-Jan./97.
2. Mark Cameron, Dept. of Microbiology and Immunology, UWO,Jan./95-May/00.
3. Henry Tung, Dept. of Microbiology and Immunology, UWO, Sept./96-Aug./99.
4. Marc Zehel, Dept. of Microbiology and Immunology, UWO, Sept./96-Aug./98.
5. Sean Prange, Dept. of Microbiology and Immunology, UWO, Sept./96-Apr./99.
6. Mike Krawetz, Dept. of Microbiology and Immunology, UWO, Sept./96-Dec./99.
7. Tracey Stephens, Dept. of Microbiol. and Immunol., UWO, May/2000-Apr./2002.
8. Melany Wagner, Dept. of Microbiology and Immunology, UWO, Jan./2002- .
9. Dalam Ly, Dept. of Microbiology and Immunology, UWO, Sept./2002- .

8. **Program Coordinator:**
Developed Program for "Production of mouse antisera directed against mouse histocompatibility antigens", Funded by Atkinson Charitable Foundation and Connaught Fund, University of Toronto, and then MRC, 1976-78.; Diabetes Seminar Series 1994-97; Co- Coordinator, Department of Microbiology and Immunology, University of Western Ontario, Seminar Series, 1994-97.

9. **Community Service (Public Lectures)**
Channel 13 Lecture on Autoimmune Diabetes; RRI Lectures on Autoimmune Diabetes; Discovery Channel Lecture on Autoimmune Diabetes; CHPL Radio Interview on Autoimmune Diabetes; Several Lectures on Autoimmune Diabetes to Fund Raising and Public Interest Parent Groups; Keynote Speaker, Shopper's Drug Mart/Juvenile Diabetes Foundation Canada "Walk for the Cure" Addresses, 1996-2002; Keynote Speaker, Juvenile Diabetes Foundation Canada Annual Board Meetings, 1997, 2000; Keynote Speaker, Juvenile Diabetes Foundation Canada Annual Fund Raising Dinner, 1998, 2000; ROB TV presentation on Diabetogen Biosciences Inc., 2000; Canadian Diabetes Association Annual Golf Fund Raising Dinner, 2001; Keynote Speaker, Canadian Diabetes Association Fund Raising Dinner, Sarnia, ON, 2002; Keynote Speaker, Canadian Diabetes Association Fund Raising Dinner, Windsor, ON, 2002; Keynote Speaker, Juvenile Diabetes Research Foundation, Fund Raising Dinner, Kitchener, ON, 2002.

10. **Roles in Conferences**

Organizer: International Symposium on "Immunological Tolerance: Impact on Transplantation and Autoimmunity", London Health Science Center, London, ON, Oct. 24-26, 1995; International Symposium on "Diabetes and Transplantation: A Common Horizon"", London Health Science Center, London, ON, April 27-28, 2001; International Taylor Award Symposium on "Diabetes in the 21st Century: Genetic and Functional Advances in the Control of Disease Susceptibility and Prevention", London Convention Center, London, ON, Nov. 6, 2002; Keystone Symposium on "Mechanism of Tolerance and its Breakdown", Keystone, CO, Jan., 2003; Scientific Program Committee, International Congress of Immunology, Montreal, PQ, Aug., 2004.

Chairman: Plenary Symposium on "Genetics and Immunology of IDDM". 75th Anniversary Symposium of the Discovery of Insulin, Toronto, ON. (Oct./96); Canadian Society of Immunology, Workshop on "Altered T Cell Signal Transduction in Pathogenic Infections Including Autoimmune Diseases", Lake Louise, AL (Mar./97); Workshop on "Novel Approaches to Autoimmune Disease Therapy", Symposium on "Molecular Farming and Molecular Medicine", London, ON (Aug./99); Keystone Symposium on "Mechanisms of Tolerance and its Breakdown". Workshop on "Regulation of Autoimmunity and Therapeutic Intervention in Autoimmune Diseases", Steamboat CO, (Apr./2000).

Member: Program Planning Committee, 75th Anniversary Symposium of the Discovery of Insulin, Toronto, ON. (Oct./96); 60th Anniversary Symposium of the Department of Microbiology and Immunology, Challenges of Microbial and Immune Diseases in the Next Millenium", London, ON (May/99); Program Committee, 2nd Annual Conference on "Molecular Farming and Molecular Medicine", London, ON, Aug./99.

GRADUATE SUPERVISION

Visiting Sabbatical Scientist

1. Dr. Michael Sefton, Department of Chemical Engineering, University of Toronto, Sept./89 - Aug./90. Project on Islet Encapsulation and Islet Beta Cell 64 K Antigen.

Research Associates

1. Peter Zucker, - PhD, U. Toronto, 1984; PDF, Ontario Cancer Inst., 1984-87; Res. Assoc., U. Miami, 1987-89; Scientist, MOTS, Univ. Hospital, 1990-95; Assist. Prof., Dept. of Med., UWO, London, ON; Res. Assoc., Autoimmunity/Diabetes Group, RRI, June/96-present.

2. Jian-Xin Gao - M.D., Suzhou Med. Coll., China, 1982; Ph.D., Dept. Immunol., Shanghai 2nd Med. U., China, 1989; PDF, Dept. Immmunol./Inflammation, Dalhousie U., 1991-94; Res. Assoc., Transplantation Immunol. Group, RRI, 1994-96; Res. Assoc., Autoimmunity/Diabetes Group, RRI, Feb./97-May/99.
(Currently Research Assist. Prof., Department of Pathology, Ohio State University)

3. Qing-Sheng Mi – M.D. Taishan Medical College, P.R.China, 1985; M.S. The Second Military Medical University, P.R. China, 1991; Ph.D., China Medical University, P.R. China, 1992. Senior Staff Scientist, Lab. Immunol., NIH, Baltimore, MD, 1996-2000. Professor/Director, Lab of Clinic Immunol., Taishan Medical College, Taian, P.R.China 1996-2000). ORDCF Research Associate, Autoimmunity/Diabetes Group, RRI, Sept./2000-Present.

Postdoctoral Fellows

1. Dr. John Harris - PhD, U. of T., May/76; MRC Fellow, Dept. of Biology, MIT, June/76 - Dec./77; NCI of Canada Fellow, BBDMR, U. of T., Jan./78 - Mar./80.
(Currently Assoc. Prof. of Oncology, London Regional Cancer Centre, London, ON)

2. Dr. Mary Laurie Phillips - Ph.D., USC, July/79; PDF, City of Hope Hospital, July/79 - July/80; Home McKechern Fellow, BBDMR, U. of T., Aug./80 - Oct./84; Res. Assoc., BBDMR, U. of T.,Nov./84 - July/86; Lecturer, BBDMR, U. of T., July/86 - Apr./88.
(Currently Director, Dept. of Pharmacol., Cytel Corp., La Jolla, CA)

3. Dr. Gary Sinclair - Ph.D., University of Calgary, Nov./80; Alberta Heritage and Savings Trust Foundation Fellow; BBDMR, U. of T., Dec./80 - July/83.
(Currently Senior Scientist., Hematology Research Group, Univ. of Calgary)

4. Dr. Phillipe Naquet - M.D., University of Aix-Marseille, Mar./83; Ph.D., University of Aix-Marseille, Dec./83; C.H. Best Foundation Fellow, BBDMR, U. of T., Apr./84 - July/86.
(Currently Assoc. Prof. of Immunology and Co-Director, Centre d'Immunologie de Marseille-Luminy, Marseille, France)

1. Dr. Nicole Bernard - Ph.D., Duke University, June, 1982; PDF, University of North Carolina, July/82 - June/84; Cancer Research Institute Fellow, BBDMR, U. of T., Aug./84 - Oct./87.
(Currently Assoc. Prof., Dept. of Medicine, Montreal General Hospital Res. Inst.)

1. Dr. John Semple - Ph.D., Queen's University, June/86; Diabetes Canada Postdoctoral Fellow, BBDMR, U. of T.,Jan./86 - June/88; Juvenile Diabetes Foundation International (JDFI) Senior Fellow, July/88 - Dec./89.
(Currently Assoc. Prof., Div. of Hematology, Dept. of Medicine, University of Toronto)

7. Dr. Michael Christie - Ph.D., Univ. of London, May/85; PDF, Hagedorn Res. Laboratory, Sept./85 - Sept./87; C.H. Best Foundation Fellow, BBDMR, U. of T., Oct./87 - Sept./89. (Currently Assoc. Prof., Dept. of Biochemistry, King's College, London, U.K.)

8. Dr. Danny Zipris - Ph.D., Bar-Ilan University, Oct./87; Diabetes Canada Fellow, BBDMR, U. of T., Oct./87 - Nov./90.
(Currently Assist. Prof., Diabetes Unit, U. Mass. Med. School, Worcester, MA)

9. Dr. Alan Lazarus - Ph.D., McGill University, Oct./87; Fonds de la Recherche en Sante du Quebec Fellow, BBDMR, U. of T., Oct./87 -Sept./92.
(Currently Assoc. Prof., Div. of Hematology, Dept. of Medicine, University of Toronto)

10. Dr. Mirko Hadzija - Ph.D., Ruder Boskovic Institute, University of Zagreb, May/83; Res. Assoc. in Experimental Diabetology, Jan./84-Sept./88; Canadian Diabetes Association (CDA) Fellow, BBDMR, U. of T., Oct./88 -Sept./91.
(Currently Assoc. Prof., Div. of Transplantation, Ruder Boskovic Inst., Univ. of Zagreb)

11. Dr. Micha Rapoport - M.D., Tel Aviv University Sackler School of Medicine, May/82; Res. Fellow, Weizmann Institute, Nov./86 - Dec./87 and Sept./89 - Dec./89; Banting and Best Diabetes Centre Hugh Sellers Fellow, BBDMR, U. of T., Aug./90 - June/91; JDFI Fellow, BBDMR, U. of T., July/91 - June/93.
(Currently Assoc. Prof., Dept. of Medicine and Head, Div. of Internal Med., Assaf Harofeh Hospital, Tel Aviv University)

12. Dr. Frederique Forquet - Ph.D., Ecole Normale Superieure de Lyon, Feb./91; JDFI Fellow, BBDMR, U. of T., Feb./91 - June/94.
(Currently Assist. Prof., Centre d'Immunologie de Marseille-Luminy, Marseille, France)

13. Dr. Andres Jaramillo - Ph.D., University of Louisville, Feb./91; C.H. Best Foundation Fellow, BBDMR, U. of T., July/91 -June/94.
(Currently Assist. Prof., Dept. of Surgery/Transplantation, Wash. Univ., St. Louis, MO)

14. Dr. Kiyotaka Kawauchi - M.D., Kyorin University School of Medicine, Tokyo, May/81; Ph.D., Tokyo Women's Medical College, Mar./88; Leukemia Research Fund Fellow, BBDMR, U. of T., July/91 - Feb./94.
(Currently Prof., Dept of Medicine/Hematology, Tokyo Women's College Hospital)

15. Dr. Bruce Gill - Ph.D., University of California, San Diego, May/92; C. H. Best Foundation Fellow, BBDMR, U. of T., Sept./92 - Aug./93; JDFI Fellow, BBDMR, U. of T. and Autoimmunity/Diabetes Group, Robarts Research Institute (RRI), Sept./93 – June/97; Lab. of Mol. Immunol. and Inflammation, RRI, July/97 – June/97.
(Deceased Sept. 99).

16. Dr. Carolyn Horrocks - Ph.D., University of Aberdeen, 1991; MRC PDF, University of Leicester, May 1991 - August 1994; PDF, Autoimmunity/Diabetes Group, RRI, Sept./94 -Aug./96.
(Currently Scientist, Stem Cell Technologies, Vancouver, BC)

17. Dr. Jian Zhang - M.D., Hunan Medical University, 1988; PDF, Assoc. Hopital Marie-Lannelongue, Oct./91 - Mar./93; Res. Fellow, CHRU de Brest, June/93 - Oct./93; JDFI Fellow, RRI, Sept./94 – Oct./99.
(Currently Assist. Prof., Dept. Orthopedic Surgery, Rush Med. Ctr., Chicago, IL)

18. Dr. Guillermo Arreaza - M.D., Central University of Venezuela, 1982; PDF, Wellesley Hospital Foundation Fellow, 1991-94; CDA Fellow, Autoimmunity/Diabetes Group,

RRI, July/95- June/97; Senior Fellow, Autoimmunity/Diabetes Group, RRI, July/97– June 2000.
(Currently Senior Scientist, Diabetogen Biosciences Inc., London, ON)

19. Dr. Konstantin Salojin - M.D., Central Scientific Research Laboratory Council of Ministry of Health, Moscow, Centre Hospitalier Universitaire Research Fellow, France, Mar./93 - Oct./94; PDF, Autoimmunity/Diabetes Group, RRI, Nov./94-Aug./96; JDFI Fellow, Autoimmunity/Diabetes Group, RRI, Sept./96 – June 2000.
(Currently Senior Scientist, Diabetogen Biosciences Inc., London, ON)

20. Dr. Isabelle Bergerot - Ph.D., Lyon 1 University, June/95; Fondation pour la Recherche Medicale Fellow, RRI, Dec./95 - June/96; CDA Fellow, Autoimmunity/Diabetes Group, RRI, July/96 –June/98.
(Currently Assistant Prof., Dept. of Endocrinology, Montpelier University, France)

21. Dr. Liljana Stevceva - M.D., University of Skopje, 1981; Ph.D., Molecular Medicine, Mucosal Inflammation and Cancer Group, John Curtin School of Medical Research, Australian National University, Oct./96; PDF, Autoimmunity/Diabetes Group, RRI, Feb. – Sept./97.
(Currently, Scientist, Trudeau Institute, Saranac Lake, NY)

22. Dr. Wei Chen – M.Sc., Hunan University, 1990; M.D., Heinrich Heine University, Sept./98; PDF, Autoimmunity/Diabetes Group, RRI, Oct./98 – Feb./99; JDRF Senior Fellow, Autoimmunity/Diabetes Group, RRI, Mar./99 - present.

23. Dr. Shayan Sharif – DVM, University of Tehran, 1991; Ph.D., University of Guelph, Oct./98; PDF, Autoimmunity/Diabetes Group, RRI, Nov./98 – June/99; CDA Fellow, Autoimmunity/Diabetes Group, RRI, July/99 - 2001.
(Currently Assist. Prof., University of Guelph, Guelph, ON)

24. Dr. Yang Wen – M.D., Hunan Medical University, 1996; Scientist, Institute of Metabolism and Endocrinology, Hunan Medical University, 1996-2000; PDF, Autoimmunity/Diabetes Group, RRI, July/2000 – June 2001; CDA Fellow, Autoimmunity/Diabetes Group, RRI, July/01 - present.

25. Dr. Shabbir Hussain – Ph.D., Ohio State University, 1998; PDF, Dept. of Pathology, Indiana University, 1998-2000; Senior PDF, Autoimmunity/Diabetes Group, RRI, Sept./2000 – June, 2001; CDA Fellow, Autoimmunity/Diabetes Group, RRI, July/01 - present.

Graduate Students

148. Dr. Gerald Prud'homme – M.D., University of Ottawa, May/77; Ph.D. Student, Institute of Immunology, University of Toronto, Sept./77 – Aug./78.

149. Julia Lin – B.Sc, University of British Columbia, May/84; Connaught Studentship award, M.Sc, Department of Immunology, University of Toronto, Sept./86.

150. Michael Bettiol – B.Sc., University of Toronto, June/81; M.Sc., University of Toronto, June/83; MRC Studentship award, Ph.D. student of Department of Immunology, University of Toronto, July/84 – Oct/86.

151. Judith Tibensky – B.Sc., University of Toronto, June/74; M.Sc., University of Toronto, Dec./76; PhD, Department of Immunology, University of Toronto, Sept./91.

152. Ying Lang – B.Med., Shandong Medical University, Mar./88; M.Sc., Department of Immunology, University of Toronto, May/92.

153. Henry Chou – B.Sc., University of Toronto, May/94; M.Sc., Department of Microbiology and Immunology, University of Western Ontario (UWO), Jan./97.

154. Mark Cameron – B.Sc., UWO, May/94; MSc Student, Department of Microbiology and Immunology, UWO, Jan./95 – Oct./96; Ph.D. Student, Department of Microbiology and Immunology, UWO, Nov./96 - present. MRC Doctoral Research Award, Apr./98 - present. UWO Graduate Tuition Scholarship, Apr. 98 – present; John Thomas Award for best graduating student in the Department of Microbiology and Immunology, UWO, May 2000.

155. Henry Tung – B.Sc., University of Waterloo, May/96: M.Sc. Student, Department of Microbiology and Immunology, UWO, Sept./96 – Aug./99. Special University Scholarship, Jan./98 – Aug./99.

156. Craig Meagher – B.Sc., University of Victoria, May/97; M.Sc. Student, Department of Microbiology and Immunology, UWO, Sept./97 – Apr./99; Ph.D. Student Department of Microbiology and Immunology, UWO, May/99 - present. Special University Scholarship, Jan./98 – present; Robarts Research Institute Special Studentship Award, Sept./99 – present; Juvenile Diabetes Foundation Canada Ron Oelbaum Diabetes Research Award, Nov./99.

157. Melany Wagner – B.Sc. (Hons. Biochemistry/Biotech.), University of Waterloo, May/01; M.Sc. Student, Department of Microbiology and Immunology, UWO, Jan../02 – present.

158. Dalam Ly - B.Sc. (Hons. Genetics.), University of Western Ontario, May/02; M.Sc. Student, Department of Microbiology and Immunology, UWO, Sept../02 – present.

Summer Students

1. Susan Friedman, 2nd year student, Department of Zoology, University of Toronto, May 1976 - August 1976.

2. Allan Fegelman, 3rd year student, Department of Zoology, University of Toronto, May 1977 - August 1977.

3. Denise Orr, 2nd year student, Department of Medicine, University of Toronto, May 1981 - August 1981.

4. Avery Nathans, 2nd year student, Department of Life Sciences, Queen's University, May 1986 - August 1986.

5. Sholeh Tavaneh, BS (Hematology), Shiraz University, Tehran (1986); May 1987 - August 1987.

6. Geeta B. Vohra, BSc (Biochemistry Specialist Program), Department of Biochemistry, University of Toronto, 1988, Juvenile Diabetes Foundation Summer Student, May 1988 - August 1988.

7. Naveen Bangia, 3rd year student, Honours BSc Immunology Specialist Program, University of Toronto, Juvenile Diabetes Foundation Summer Student, May 1989 - August 1989.

8. Andre Lipinski, 2nd year student, BSc, McMaster University, Juvenile Diabetes Foundation Summer Student, May 1990 - August 1990.

9. Lingli Ma, 3rd year student, BSc Life Sciences Program, Queen's University, Juvenile Diabetes Foundation International Summer Student, May 1992 - August 1992.

10. Kevin Laupland, BSc, University of Victoria, 1st year Medicine, University of Toronto, Juvenile Diabetes Foundation Summer Student, June 1993 - August 1993; September 1993 - December 1993.

11. Dan Hardy, University of Waterloo Biology Co-op Student, Student Training Research Program (STRP), May 1995 - August 1995.

12. Sean Bagshaw, BSc, The University of Western Ontario, Dr. Theodor Ackermann Scholarship in Diabetes Research, May 1996 - August 1996.

13. Craig Meagher, BSc, University of Victoria, May 1997; Dr. Theodor Ackermann Scholarship in Diabetes Research, May 1998 - August 1998.

14. Tisha Joy, Dr. Theodor Ackermann Scholarship in Diabetes Research, June 1999 - August 1999.

15. Bindee Kuriya, Hargreaves Summer Student, Faculty of Medicine, The University of Western Ontario, May 1999 - August 1999.

16. Jitin Sondi, 3rd year student, Hons. Biology Program, University of Western Ontario, May 2000 - August 2000.

17. Lamis Hammoud, 3rd year student, Hons. Biology Program, University of Western Ontario, May 2000 - August 2000.

18. Mitchell Sivilotti, 4th year student, Hons. Genetics Program, University of Western Ontario, May 2000 - August 2000.

19. Mitchell Sivilotti, B.Sc. Hons. Genetics, University of Western Ontario, May 2001 - August 2001.

20. Dalam Ly, 3rd and 4th year student, Hons. Biology Program, University of Western Ontario, May-Aug. 2000/May-Aug. 2001; 4th year Biochem 483 Project Student, Sept. 2001- Mar./2002.

21. Megan McGarry, 4th year student, Hons. Genetics Program, University of Western Ontario, May 2001 - August 2001.

Teaching

(University of Toronto)

1. Immunology Laboratory Course (to 2nd year Medical Students) - Demonstrator and Tutorial Session Leader
   Course: IMM 1020 F.S.; Dates: Nov.-Dec. 1976; Oct.-Dec. 1977; Oct.-Dec. 1978; Oct.-Dec. 1979; Time: 20 hr/yr
2. Immunogenetics Course (to graduate students) - co-ordinated and taught Histocompatibility Genetics Section (12 hr)
   Course: IMM 1018, F.S.; Date: Feb.-April 1977; Time: 6 hr.
3. Biochemistry of Differentiation (to graduate students) - lecture on Immunology and Differentiation
   Course: BCH 2021, FS.; Date: Mar. 1977; Time: 2 hr.
4. Communications Between Cells - coordinated and taught section on the Genetic Control of the Immune Response
   Course: IMM 1018 F.S.; Date: Sept. - Dec.1980; Time: 12 hr.
5. Special Topics in Immunology - lecture on Immune Response Genes
   Course: IMM 2021 L; Date: Feb. 1981; Time: 2 hr.
6. Special Topics in Immunology - section on Molecular Genetic and Functional Analysis of the Major Histocompatibility Complex
   Course: IMM 2021 L; Date: May-June 1984; Time: 6 hr.
7. Recent Advances in Cellular Immunology - section on B Cell Activation
   Course: IMM 1016 H; Date: Nov.-Dec. 1984; Time: 8 hr.
8. Special Topics in Immunology - section on Biochemistry of Antigen Presentation
   Course: IMM 2021 L; Date: Jan. 1985; Time: 2 hr.
9. Recent Advances in Clinical Immunology - section on Human T Cell Cloning
   Course: IMM 1020 H; Date: Feb. 1985; Time: 2 hr.
10. Recent Advances in Molecular Immunology - course coordinator -section on MHC Genes
    Course: IMM 1017 H; Date: Jan.-Apr. 1986; Time: 24 hr.
11. Recent Advances in Molecular Immunology - section on Antigen Processing and MHC Polymorphism.
    Course: IMM 1017 H; Date: Apr. 1990; Time: 4 hr.
12. Recent Advances in Molecular Immunology - section on Antigen Processing and Presentation.
    Course: IMM 1017 H; Date: Jan. 1991; Time: 4 hr.
13. Recent Advances in Molecular Immunology - section on T Cell Activation and Signal Transduction.
    Course: IMM 1017 H; Date: Dec. 1991; Time: 6 hr.
14. Recent Advances in Immunology - section on Cytokines and T Cell Signalling
    Course: IMM 1016H, Part I; Date: Jan. 1993; Time: 4 hr.

(University of Western Ontario)

1. Immunology - section on Antigen Processing
   Course: IMM 357A; Date: Oct. 1994; Time: 2 hr.
2. Advanced Immunology - section on Autoimmunity and Type I Diabetes
   Course: IMM 473A; Date: Nov. 1994; Time: 2 hr.

3. Clinical Immunology - section on Immunology of Diabetes Mellitus
   Course: MEDS IV; Date: Mar. 1995; Time: 1 hr.
4. Advanced Immunology - section on Autoimmunity and Type I Diabetes
   Course: IMM 473A; Date: Nov. 1995; Time: 2 hr.
5. Clinical Immunology - section on Immunology of Diabetes Mellitus
   Course: MEDS IV; Date: Apr. 1996; Time: 1 hr
6. Clinical Immunology - section on Immunology of Diabetes Mellitus
   Course: MEDS IV; Date: Mar./95; Time: 2 hr (6 students)
7. Advanced Immunology - section on Autoimmunity and Type I Diabetes
   Course: IMM 473A; Date: Nov./95; Time: 2 hr (15 students)
8. Clinical Immunology - section on Immunology of Diabetes Mellitus
   Course: MEDS IV; Date: Mar./96; Time: 2 hr (8 students)
9. Current Concepts in Immunology - section on Cytokines and Effector Functions
   Course Coordinator: IMM 512b; Date: Jan.-Apr./98; Time: 9 hr (13 students)
10. Current Concepts in Immunology - section on NKT Cells and Immunoregulation
    Course: IMM 512b; Date: Jan.-Apr./2000; Time: 9 hr (11 students)
11. Current Concepts in Immunology - section on NKT Cells and Immunoregulation
    Course: IMM 512b; Date: Jan.-Apr./2001; Time: 9 hr (13 students)

12. Research

1. **Current Grant Support (Principal investigator on each grant)**

Title	Agency	Period	Amount/yr
Antigen Specific Therapy of Type 1 Diabetes with Pro(Insulin)	CIHR	2001-04	118,700
Regulatory Autoreactive T Cells in Type 1 Diabetes	CIHR/JDRF	1996-02	90,000
Role of NKT Cells in Protection Against the Onset and Recurrence of Type 1 Diabetes.	JDRF	2001-04	240,000
Role of T Cell Resistance to Activation-Induced Apoptosis In Susceptibility to Type 1 Diabetes	CDA	2000-02	60,000
Prolongation of Islet Transplants by NKT Cell Activation Therapy	MOTP	2000-02	60,000

CIHR, Canadian Institutes of Health Research; JDRF, Juvenile Diabetes Research Foundation; CDA, Canadian Diabetes Association; MOTP, Multi Organ Transplantation Program (London Health Sci. Ctr).

2. **Pending Grant Support**

Title	Agency	Period	Amount/yr
Role of IL-16 in the Pathogenesis of Type I Diabetes	CIHR	2003-06	138,695
Role of B Cells in the Pathogenesis of Type 1 Diabetes	CDA	2003-06	75,000
Isolation f Early NKT Cell Progenitors and Their Role in Type 1 Diabetes (Co-PI with Dr. J. Verdi)	NIH	2003-08	250,000

3. **Research Contracts:**

Ex-Vivo Cell Therapy of Type I Diabetes	Hemosol Inc.	1997-99	100,000
Expression of IL-4 in Transgenic Low-Nicotine Tobacco	Agri. Canada	1996-98	50,000

INVITED LECTURES (1985-2002)

1. Seminars

1. Dept. of Microbiology and Immunology, University of Rochester
2. Dept. of Pathology, Queen's University
3. McGill Cancer Centre, McGill University
4. Dept. of Rheumatic Diseases, Hospital for Joint Diseases, New York, N.Y.
5. Dept. of Clinical Medicine, John Radcliffe Hospital, Oxford, U.K.
6. Dept. of Anatomy, University of Toronto.
7. Dept. of Medical Biophysics, University of Toronto.
8. Dept. of Immunology, University of Nice, Nice, France.
9. Centre d'Immunologie de Marseille - Luminy, Marseille, France
10. Banting and Best Diabetes Centre, University of Toronto.
11. Division of Endocrinology, Hospital for Sick Children
12. Division of Immunology, Metabolism Branch, NCI/NIH, Bethesda, MD.
13. Dept. of Microbiology and Immunology, University of Western Ontario.
14. John Robarts Centre for Research, University of Western Ontario.
15. Division of Nephrology, Toronto General Hospital
16. Division of Immunology, Smith Kline and French, Philadelphia.
17. Clinical Research Institute of Montreal, Division of Molecular Immunology.
18. Dept. of Microbiology and Immunology, McGill University.
19. Division of Autoimmunity, Bayer-Miles, West Haven, CT.
20. Alberta Heritage Savings Trust Fund Visiting Lecturer, Department of Microbiology and Infectious Disease, Division of Virology, Faculty of Medicine, University of Calgary.
21. Dept. of Pediatrics, National Jewish Ctr. for Immunology and Respiratory Med., Denver.
22. Immunology Res. Group, Dept. of Microbiology and Infectious Disease, Univ. of Calgary.
23. Membrane and Cell Biology Group, Hospital for Sick Children, Toronto.
24. Dept. of Microbiology and Immunology, Stanford University, Stanford, CA.
25. Dept. of Microbiology and Immunology, Duke University, Durham, NC.
26. Division of Rheumatology, Wellesley Hospital, Toronto.
27. Division of Immunology, Montreal Children's Hospital.
28. Division of Basic Medical Sciences, Memorial University, St. John's, Nfld (1989).
29. City-wide Endocrine Rounds, University of Toronto (1989).
30. Dept. of Microbiology and Immunology, University of Rochester, Rochester, NY (1990).
31. Dept. of Microbiology and Immunology, Northwestern University, Chicago, IL (1990).
32. Dept. of Immunology, University of Toronto (1990).
33. Dept. of Medicine, Tokyo Women's College Hospital, Tokyo (1991).
34. Dept. of Microbiology and Immunology, University of North Carolina, Chapel Hill, NC (1991).
35. Dept. of Medicine, North Shore Univ. Hospital, Cornell Univ. Med. Coll., Manhasset, NY (1991).
36. Laboratory of Immunology, NIAID, NIH, Bethesda, MD (1992).
37. Department of Immunology, University of Alberta, Edmonton, AL (1992).
38. Department of Microbiology and Immunology, University of Western Ontario, London, ON (1992).

39. Virginia Mason Research Center, University of Washington, Seattle, WA (1992).
40. Department of Microbiology and Immunology, UCLA, Los Angeles, CA (1993).
41. Barbara Davis Diabetes Center, University of Colorado, Denver, CO (1993).
42. Dept. of Pathology, New York University, New York, NY (1993).
43. Dept. of Biochemistry, University of Texas, San Antonio, TX (1993).
44. Centre d'Immunologie, Toulouse, France (1993).
45. Dept. of Immunology, Hopital Necker, Paris, France (1994).
46. Dept. of Immunology, Cleveland Clinic, Cleveland, OH (1994).
47. Dept. of Experimental Oncology, London Regional Cancer Centre, London, Ontario (1995).
48. Dept. of Physiology, University of Western Ontario (1995).
49. Dept. of Anatomy, University of Western Ontario (1995).
50. Department of Molecular Genetics and Immunology, UCLA, Los Angeles, CA (1995).
51. Banting and Best Diabetes Center, University of Toronto, Toronto, ON (1995).
52. Laboratory of Experimental Immunology, NCI/NIH, Bethesda, MD (1996).
53. Dept. of Pathology and Laboratory Medicine, Univ. of Florida, Gainesville, FL (1997).
54. Dept. of Microbiology and Immunology, Wayne State Univ., Detroit, MI (1997).
55. Department of Immunology, American Red Cross, Bethesda, MD (1997).
56. Immunology Research Group, Univ. of Calgary, Calgary, AL (1997).
57. Dept. of Immunology, Univ. of Toronto, Toronto, ON (1997).
58. Dept. of Biology, University of California San Diego, San Diego, CA (1998).
59. Dept. of Pediatrics, Medical College of Wisconsin, Milwaukee, WI (1998).
60. Dept. of Pediatrics and Immunogenetics, University of Pittsburgh, Pittsburgh, PA (1998).
61. Sansum Medical Research Institute, Santa Barbara, CA (1999).
62. Dept. of Medicine/Rheumatology, Columbia University, New York, NY (1999).
63. Centre d'Immunologie de Marseille-Luminy, Marseille, France (1999).
64. Department of Biochemistry, Signal Transduction Seminar Series, UWO (1999).
65. Diabetes Center, Cornell Medical Center, New York. NY (1999).
66. Endocrinology Rounds, London Health Science Center (2000).
67. Barbara Davis Diabetes Center, University of Colorado (2000).
68. Diabetes Center, University of Massachusetts (2000).
69. Sloan-Kettering Memorial Institute, New York, NY (2000).
70. La Jolla Institute for Allergy and Immunology, La Jolla, CA (2000).
71. Rush Medical College, Chicago, IL (2001).
72. Barbara Davis Diabetes Center, University of Colorado (2001).
73. La Jolla Institute for Allergy and Immunology, La Jolla, CA (2001).
74. Dept. of Pathology, Ohio State University (2002)

Public Lectures (1994-2002)

1. Channel 13 Lecture on Autoimmune Diabetes (1994)
2. Robarts Research Institute Series (2) on Autoimmune Diabetes (1994, 1995)
3. Discovery Channel Lecture on Autoimmune Diabetes (1995)
4. CHPL Radio Interview on Autoimmune Diabetes (1995)
5. Keynote Address to Nurses Association of Ontario, Sarnia, ON (1999)
6. Several Lectures on Autoimmune Diabetes to Fund Raising (JDRFI, CDA, Shopper's Drug Mart, etc.) and Public Interest Groups (1995-2002)

6. Keynote Address to Canadian Diabetes Association, Sarnia, ON and Windsor, ON (2002)
7. Keynote Address to Juvenile Diabetes Research Foundation, Kitchener, ON (2002)

Presentations at National and International Meetings

1. Symposium on "Mediators of Immune Regulation and Immunotherapy", Univ. of Western Ontario, London, Ontario. Co-organized this Symposium and co-edited this volume (June/85).
2. Symposium on "Antigen Presentation", CFBS Meeting, University of Toronto, Toronto (June/85).
3. 6th Ir Gene Workshop on "Immune Regulation", Trinity College, Oxford, U.K. (Oct./85)
4. Minisymposium on "Antigen Presentation". FASEB Meeting, St. Louis, MO. (Apr./86).
5. Satellite Symposium of Sixth International Congress of Immunology on "Immunology of Diabetes", Edmonton, Alta. (June/86).
6. Sixth International Congress of Immunology, Symposium on "Antigen Processing and Presentation". Toronto. (June/86).
7. Fifth HLA and H-2 Cloning Workshop. Les Avants, Switzerland. (Oct./86).
8. Reticuloendothelial International Symposium on "Antigen Presenting Cells: Diversity, Differentiation, and Regulation. Symposium talk in Session on "Requirements for Antigen Processing and Presentation". (Mar./87).
9. UCLA Symposia on Molecular and Cellular Biology. "The T Cell Receptor". Workshop on "Antigen Presentation". Keystone, Colorado. (Apr./87).
10. IX Steno Symposium on "Mechanisms of Clearance and Processing of Protein Molecules". Symposium talk in Session on "Molecular Mechanisms of Antigen Processing and Presentation". Hagedorn Laboratory, Copenhagen. (May/87).
11. 50th Anniversary Symposium on H-2 Gene Complex. Talk on "Localization of Antigen-Ia Complexes in Antigen Presenting Cells". Bar Harbour, ME. (June/87).
12. Symposium on "MHC Specific Antibodies Induced by Foreign Antigen". Talk on "Antigen-Ia Complexes: Are They Formed Intracellularly or at the Cell Surface? Amsterdam (Oct./87).
13. Workshop on "Molecular Basis of Antigen Presentation by MHC Molecules". Talk on "Interaction of Insulin Peptides with MHC Class II Molecules". Paris (Nov./87).
14. Symposium on "Autoimmunity". Talk on "T Cell Autoreactivity to Insulin in Type I Diabetes". Toronto Western Hospital, Toronto (June/88).
15. Gordon Conference on "Immunochemistry and Immunobiology". Talk on "Processing of Insulin In Situ by B Lymphocytes". New Hampshire (July/88).
16. Canadian Society of Immunology Symposium on T Suppressor Cells. Symposium Chairman. Talk on "T Suppressor cells and Tolerance". Lake Louise, ALTA (Mar./89).
17. Cold Spring Harbor Symposium on "Immune Recognition". Talk on "Endocytic Pathway of Processing and Presentation of Insulin by Antigen Presenting B Cells". Cold Spring Harbor, NY (June/89).
18. 20th Anniversary Meeting of Insulin Crystal Structure Determination. Talk on "Immune Recognition of Insulin." York, England. (Aug./89)
19. Juvenile Diabetes Foundation Workshop on NOD Mouse. Talk on "T Cell Development in the NOD Mouse". Scottsdale, Arizona (Oct./89).

20. 10th International Workshop on Immunology of Diabetes. Talk on "Aberrant Intrathymic T Cell Development and Clonal Deletion in NOD Mice". Jerusalem, Israel (Mar./90).
21. 7th International HLA/H-2 Workshop. Talk on "Antigen Processing and Self Tolerance". Schloss Elmau, Germany (May/90).
22. European Network of Immunology Institutes 1990 Conference, Immune Functions At The Molecular Level. Talk on "Biochemical Evidence that Different MHC Class II - Binding Peptides of an Antigen are Present on Different Thymic Antigen Presenting Cells". Les Embiez, France (May/90).
23. Workshop on "Ir Genes, From Biology to Medicine."Talk on "Evidence for Altered Ligand Hypothesis of Thymic Selection". Paris, France (Nov./90).
24. Keystone Symposium on "Self-Reactivity". Workshop Talks on "Naturally Processed Peptides on Thymic APCs" and "Thymic T Cell Anergy in Prediabetic NOD Mice". Keystone, Colorado (Jan./91).
25. Cancer Research Institute (New York). Meeting on "Molecular and Cellular Biology of Antigen Processing and Presentation". Talk on "Antigen Processing and Thymic Selection". New York (May/91).
26. 11th International Histocompatibility Workshop and Conference, Symposium Talk on "Autoimmune Type I Diabetes: Altered Thymic T Cell Signalling in NOD Mice, a Possible Early Diagnostic Indicator of Predisposition to Disease". Yokohama Japan (Nov./91).
27. 11th International Immunology and Diabetes Workshop, Talk on "Defective T Cell Activation on NOD Mice". Nagasaki, Japan (Nov./91).
28. Symposium on "Self Tolerance, Autoimmunity and Therapy", Talk on "T Cell Unresponsiveness and Idd Susceptibility Genes in Type I Diabetes". Fukuoka Japan (Nov./91).
29. Canadian Society of Immunology Workshop on Autoimmunity, Talk on "How Can Multiple Idd Susceptibility Genes Influence the Breakdown of Tolerance in Type I Diabetes?" Mont Rolland, Quebec (Mar./92).
30. 8th International HLA/H-2 Workshop. Talk on "Influence of MHC Class II Molecules on Antigen Processing". Jeckyl Island, GA. (Apr./92)
31. International Conference on Molecular and Cellular Aspects of Self-Reactivity and Autoimmune Disease, Symposium Talk on "IL-4 Reverses Thymic T Cell Anergy and Prevents the Onset of Diabetes in NOD Mice". Taormina, Sicily, Italy (June/92).
32. Molecular Aspects of Endocrine Autoimmunity, Symposium Talk on "Defective Thymic T Cell Signalling in Pre-diabetic NOD Mice.". Mainz, Germany (Aug./92).
33. 8th International Congress of Immunology, Workshop Talk on "Defective Thymic T Cell Activation in NOD Mice: A Possible Diagnostic Indicator of Predisposition to Disease".
34. Budapest, Hungary (Aug./92).
35. 12th International Immunology and Diabetes Workshop, Talk on "IL-4 Reverses Thymic T Cell Anergy and Prevents the Onset of Diabetes in NOD Mice". Orlando, FL (Apr./93)
36. 9th International HLA/H-2 Workshop, Talk on "Naturally Processed Heterodimeric Disulfide-Linked Insulin Peptides Bind to MHC Class II Molecules on Thymic Epithelial Cells". Garda, Italy (May/94)
37. 13th International Immunology and Diabetes Workshop, Talk on "Thymic T Cell Anergy in NOD Mice is Reversed By Costimulation Via CD28". Chantilly, France (May/94)

38. 15th International Diabetes Federation Congress, Symposium, Talk on "Anti-Inflammatory Role of IL-4 and Th2 Cell Responses in the Protection Against Type I Diabetes". Kobe, Japan (Nov./94).
39. 1st International Workshop on Antigen Processing and Presentation, Talk on "Role of Altered APC Function and Apoptosis in IDDM Susceptibility in NOD Mice". Oxnard, CA (Dec./95).
40. Canadian Society of Immunology Workshop on Autoimmunity, Talk on "Role of IL-4 in the Pathogenesis of Type I Diabetes". Chantecler, Quebec (Mar./96).
41. Keystone Symposium on "Lymphocyte Activation". Talk on "Role of IL-4 in the Pathogenesis of Type I Diabetes". Hilton Head, SC (Mar./96).
42. 75th Anniversary Symposium of the Discovery of Insulin, Chairman, Plenary Symposium on "Genetics and Immunology of IDDM". Toronto, ON. (Oct./96).
43. Canadian Society of Immunology, Co-Chair of Workshop on Altered T Cell Signal Transduction in Pathogenic Infections Including Autoimmune Diseases. Talk on "Tyrosine Hyperphosphorylation of the TCR/CD3 Complex and Deficient Ras GDP Releasing Factor Activity Mediate T Cell Unresponsiveness in NOD Mice". Lake Louise, AL (Mar./97).
44. Keystone Symposium on "Tolerance and Autoimmunity". Workshops on Autoimmune Diabetes. Talks on "Prevention of IDDM by Treatment with IL-4, Anti-CD28 and Insulin", and "Tyrosine Hyperphosphorylation of the TCR/CD3 Complex and Deficient Ras GDP Releasing Factor Activity Mediate T Cell Unresponsiveness in NOD Mice. Keystone, CO (Apr./97).
45. Ninth Annual Symposium on Immunobiology of Proteins and Peptides. Invited Symposium Talk on "Cytokine-, Costimulation- and Auroantigen Mediated Therapy of IDDM". Whistler, BC (May/97).
46. FASEB Summer Conference on "Autoimmunity". Invited Symposium Talk on "Cytokine-, Costimulation- and Autoantigen-Mediated Therapy of IDDM". Saxton's River, VT (June/97).
47. Workshop on "Regulation of Autoimmunity: Diabetes, EAE/MS, and Arthritis". Talks on "Prevention of IDDM by Treatment with IL-4, Anti-CD28 and Insulin", and "Tyrosine Hyperphosphorylation of the TCR/CD3 Complex and Deficient Ras GDP Releasing Factor Activity Mediate T Cell Unresponsiveness in NOD Mice". Genoa, Italy (Sept./97).
48. First Annual Meeting of the Canadian Diabetes Association. Invited Symposium Talk on "Immune Dysregulation Elicits IDDM in NOD Mice". London, Ontario (Oct./97).
49. Toronto Diabetes Association. Invited Symposium Talk on "Immune Modulation in Prevention of IDDM". Toronto, Ontario (May/98).
50. European Association for the Study of Diabetes and Juvenile Diabetes Foundation International Workshop on "Manipulating the Immune Response for Prevention and Cure of Insulin Dependent Diabetes". Invited Symposium Talk on "Immune Modulation in Prevention of IDDM". Oxford, U.K. (Sept./98).
51. Keynote Speaker, Juvenile Diabetes Foundation Canada Annual Board meeting in 1997 and Marketing Campaign meeting in 1998.
52. INSERM/CNRS Symposium on "Cellular and Molecular Immune Responses" – Tribute to Claude de Preval. Invited Symposium Talk on " Novel Approaches to Prevention of Autoimmune Type I Diabetes". Toulouse, France. (Dec./98).
53. Keystone Symposium on "Tolerance and Autoimmunity". Workshop on Autoimmune Disease. Talk on "IL-4 Treatment Modulates the Role of MIP-1α in the Pathogenesis of Autoimmune Diabetes. Keystone, CO (Mar./99).

54. Symposium on Autoimmune Diseases. Invited talk on "Immune Modulation in Type I Diabetes". Emerald Lake, B.C. (Sept./99).
55. 4th Congress of the Immunology of Diabetes Society. Presentation on "Role of Chemokines in Susceptibility to Type I Diabetes", Fiuggi, Italy (Oct./99).
56. Keystone Symposium on "Mechanisms of Immunologic Tolerance and its Breakdown". Chairman, Workshop on "Regulation of Autoimmunity and Therapeutic Intervention in Autoimmune Disease". Talk on "Regulation of Autoimmune Type I Diabetes by T Cells and APCs". Steamboat Springs, CO (Apr./2000).
57. JDFI Workshop on "Predicting Diabetes & Response to Preventive Therapy: Can Individual Animals Provide Lessons for Man". Talks on "Regulatory NKT Cells" and "Antigen-Specific Therapy of Type 1 Diabetes with Proinsulin". Winter Park, CO (Oct. 5-7/2000).
58. 5th Congress of the Immunology of Diabetes Society. Symposium Presentation on "Role of NKT Cells in Prevention of Type I Diabetes. Chennai (Madras), India (Feb. 13-16/2001).
59. Federation of Clinical Immunology Societies (FOCIS) First Annual Meeting. Symposium talk on " Activation of NKT Cells by Alpha-GalactosylCeramide Treatment Prevents the Onset of Type 1 Diabetes and Recurrence after Islet Transplantation". Boston, MA (May 4-7/2001).
60. American Association of Diabetes. Symposium talk on "Gene Therapy of Type 1 Diabetes". Philadelphia, PA (June 22-26/2001).
61. International Conference on "Emerging Technologies in Gene and Drug Therapy". Symposium talk on "Biolistic Mediated Interleukin-4 Gene Transfer Prevents the Onset of Type 1 Diabetes". Corfu, Greece (Aug.25-31/2001).
62. Novartis Foundation Symposium 252 on "Generation Effector Functions of Regulatory lymphocytes. Symposium talk on "CD1d Restricted NKT Regulatory cells: Functional Genomic Analyses Provide New Insights into Mechanism of Protection Against Type 1 Diabetes". London, UK (July 9-11, 2002).
63. British Royal Society of Medicine. Symposium talk on "Regulation of Susceptibility to Type 1 Diabetes by NKT Cells". London, UK (July 12/2002).
64. 6th Congress of the Immunology of Diabetes Society. Symposium talk on "Counter-regulatory roles of IL-16 and MIP-1β in the pathogenesis of type 1 diabetes". Copper Mountain, CO (Oct. 3-6/2002).
65. CD1 and NKT Cell Workshop. Symposium talk on "NKT Regulatory Cells: Functional Genomic Analyses Provide New Insights into their Mechanism of Protection Against Type 1 Diabetes. Woods Hole, MA (Nov. 5-8/2002).
66. Taylor Award Symposium on "Diabetes in the 21st Century. Genetic and Functional Advances to the Prevention and Treatment of Type 1 Diabetes". Symposium talk on "Genetic Control of Susceptibility to the Pathogenesis of Type 1 diabetes". London, ON. (Nov. 6/2002).
67. Keystone Symposium on "Mechanisms of Immunologic Tolerance and its Breakdown. Symposium talk on Protection Against Type 1 Diabetes by Regulation of NKT Cell, IL-16 and CCL4 Activity. Snowbird, Utah (Jan. 7-13/2003).

PUBLICATIONS (1969-2002)

1. Davis, B.K., Delovitch, T.L., and Sehon, A.H. (1969). Isolation of Polysomes from Mouse Plasmacytomas. Nature 222: 172-174.

2. Holme, G., Delovitch, T.L., Boyd, S.L., and Sehon, A.H. (1971). The Immunochemical Precipitation of Polyribosomes. Biochim. Biophys. Acta 247: 104-108.

3. Boyd, S.L., Delovitch, T.L., Holme, G., and Sehon, A.H. (1971). Isolation of Messenger-Like Ribonucleic Acid from Immunochemically-Precipitated Polyribosomes. Biochem. J. 125: 99P-100P.

4. Delovitch, T.L., Davis, B.K., Holme, G., and Sehon, A.H. (1972). Isolation of Messenger-Like RNA from Immunochemically Separated Polyribosomes. J. Mol. Biol. 69: 373-386.

5. Delovitch, T.L. and Baglioni, C. (1972). Estimation of the Reiteration of Ig Genes by RNA-DNA Hybridization. Scand. J. Immunol. 1: 284-285.

6. Baglioni, C., Pemberton, R., and Delovitch, T.L. (1972). Presence of Polyadenylic Acid Sequences in RNA of Membrane-Bound Polyribosomes. FEBS Letters 26: 320-322.

7. Delovitch, T.L., Boyd, S.L., Tsay, H.M., Holme, G., and Sehon, A.H. (1973). The Specific Immunoprecipitation of Polyribosomes Synthesizing an Immunoglobulin Light Chain. Biochim. Biophys. Acta 299: 621-633.

8. Delovitch, T.L. and Baglioni, C. (1973). Estimation of Light-Chain Gene Reiteration of Mouse Immunoglobulin by DNA-RNA Hybridization. Proc. Nat. Acad. Sci. USA 70: 173-178.

9. Delovitch, T.L. and Baglioni, C. (1973) Immunoglobulin Genes A Test of Somatic Vs. Germ Line Hypothesis by RNA/DNA Hybridization. In: Cold Spring Harbor Symposium on Quantitative Biology XXXVIII: 739-751.

10. McDevitt, H.O., Bechtol, K.B., Hammerling, G.J., Lonai, P., and Delovitch, T.L. (1974). Ir Genes and Antigen Recognition. In: The Immune System: Genes, Receptors, Signals. Third ICN-UCLA Symposium on Molecular Biology. E.E. Sercarz, A.R. Williamson, and C.F. Fox, Eds. Academic Press, New York. pp. 597-632.

11. Delovitch, T.L. and McDevitt, H.O. (1975). Isolation and Characterization of Murine Ia Antigens. Immunogenetics 2: 39-52.

12. Press, J.L., Klinman, N.R., Henry, C., Wofsy, L., Delovitch, T.L., and McDevitt, H.O. (1975). Ia Antigens on B Cells: Relationship to B Cell Precursor Function and to Surface Immunoglobulin. In: Membrane Receptors of Lymphocytes. M. Seligmann, J.L. Preud'homme, and F.M. Kourilsky, Eds. North Holland Publishing Company, Amsterdam: The Netherlands. pp. 247-258.

13. Delovitch, T.L., Murphy, D.B., and McDevitt, H.O. (1976). Evidence for the Association of Specificity Ia. 3 with an *I-A*. Region Molecule. In: Role of the Products of the Histocompatibility Complex in Immune Responses. D.H. Katz and B. Benacerraf, Eds. Academic Press, New York. pp. 87-90.

14. McDevitt, H.O., Delovitch, T.L., Press, J.L., and Murphy, D.B. (1976). Genetic and Functional Analysis of the Ia Antigens: Their Possible Role in Regulating the Immune Response. Transplant. Rev. 30: 197-235.

15. McDevitt, H.O., Delovitch, T.L., and Press, J.L. (1977). Functional and Genetic Analysis of Ia Antigens. In: Cold Spring Harbor Symposium on Quantitative Biology XLI: 489-496.

16. Delovitch, T.L. and McDevitt, H.O. (1977). In Vitro Analysis of Allogeneic Lymphocyte Interaction. I. Characterization and Cellular Origin of an Ia-Positive Helper Factor-Allogeneic Effect Factor. J. Exp. Med. 146: 1019-1032.

17. Delovitch, T.L., Murphy, D.B., and McDevitt, H.O. (1977). Immunochemical Evidence for Three Ia Loci in the *I*-Region of the *H-2* Complex. J. Exp. Med. 146: 1549-1560.

18. Delovitch, T.L., Press, J.L., and McDevitt, H.O. (1978). Expression of Murine Ia Antigens During Embryonic Development. J. Immunol. 120: 818-824.

19. Delovitch, T.L., Murphy, D.B., and McDevitt, H.O. (1978). Evidence for the Presence of an Ia Molecule Determined by Each of the Ia-3 and Ia-5 Loci. In: Ir Genes and Ia Antigens. H.O. McDevitt, Ed. Academic Press, New York. pp. 29-35.

20. Delovitch, T.L. (1978). Role of an Ia-Positive Allogenic Effect Factor in B-Cell Activation. In: Ir Genes and Ia Antigens. H.O. McDevitt, Ed. Academic Press, New York. pp. 503-516.

21. Delovitch, T.L., Biggin, J., and Fung, F.-Y. (1978). In Vitro Analysis of Allogeneic Lymphocyte Interaction. II. *I*-Region Control of the Activity of a B-Cell Derived *H-2* Restricted Allogeneic Effect Factor and Its Receptor During B-Cell Activation. J. Exp. Med. 147: 1198-1212.

22. Delovitch, T.L. and Sohn, U. (1979). I Region Control of the Activity of Allogeneic Effect Factor. In: Proceedings of the 12th International Leukocyte Culture Conference. Cell Biology and Immunology of Leukocyte Function. M.R. Quastel, Ed. Academic Press, New York. pp. 339-347.

23. Prud'Homme, G.J., Sohn, U., and Delovitch, T.L. (1979). The Role of H-2 and Ia Antigens in Graft-Versus-Host Reactions (GVHR). Presence of Host Alloantigens on Donor Cells After GVHR and Suppression of GVHR With an Anti-Ia Antiserum Against Host Ia Antigens. J. Exp. Med. 149: 137-149.

24. Barber, B.H. and Delovitch, T.L. (1978). The Identification of Actin as a Major Lymphocyte Component. J. Immunol. 122: 320-325.

25. Delovitch, T.L., Fegelman, A., Barber, B.H., and Frelinger, J.A. (1979). Immunochemical Characterization of the Ly-8.2 Murine Lymphocyte Alloantigen: Possible Relationship to Actin. J. Immunol. 122: 326-333.

26. Rowden, G., Phillips, T.M., and Delovitch, T.L. (1978). Expression of Ia Antigens by Murine Keratinizing Epithelial Langerhans Cells. Immunogenetics 7: 465-478.

27. Zimmerman, B., Tsui, F., and Delovitch, T.L. (1979). Immunosuppressive ALS. II. Antibody to Ia Antigens in Heterologous Anti-Lymphocyte Serum. Immunology 37: 179-186.

28. Delovitch, T.L. and Sohn, U. (1979). *In Vitro* Analysis of Allogeneic Lymphocyte Interaction. III. Generation of a Helper Allogeneic Effect Factor (AEF) Across an *I-J* Subregion Disparity. J. Immunol. 122: 1528-1534.

29. Delovitch, T.L. and Sohn, U. (1979). *In Vitro* Analysis of Allogeneic Lymphocyte Interaction. IV. Dual Recognition of B Cell-Associated *Mls* Locus and *I*-Region Determinants by Helper Allogeneic Effect Factor (AEF) Generated Across a Minor *H* Locus Disparity. J. Immunol. 123: 121-127.

30. Delovitch, T.L. and Barber, B.H. (1979). Evidence for Two Homologous, but Non-Identical Ia Molecules Determined by the *I-EC* Subregion. J. Exp. Med 150: 100-107.

31. Delovitch, T.L. and Falk, J.A. (1979). Evidence for Structural Homology Between Murine and Human Ia Antigens. Immunogenetics 8: 405-418.

32. Delovitch, T.L., Prud'Homme, G.J., and Sohn, U. (1980). Ia Phenotype and Immunosuppression by Anti-Ia of Alloreactive Donor T Cells in a Graft-Versus-Host Response. In: The Biological Basis for Immunodeficiency Disease. E.W. Gelfand and H. M. Dosch, Eds. Raven Press, New York. p. 111-123.

33. Delovitch, T.L. (1980). Regulation of B Cell Activation by Allogeneic Effect Factor (AEF). In: Strategies of Immune Regulation. E. Sercarz and A.J. Cunningham, Eds. Academic Press, New York. pp. 329-330.

34. Hooper, D.C., Delovitch, T.L., Wigzell, H., and Murgita, R.A. (1980). Analysis of an Immunoregulatory Suppressor T Cell System in Newborn Mice. In: Proceedings of the 13th International Leukocyte Culture Conference. J.G. Kaplan, A. Boyn:on, D. Forsdyke, and L.M. Jerry, Eds. Elsevier/North Holland Biomedical Press, Amsterdam. pp. 676-679.

35. Shaw, J., Caplan, B., Paetkau, V., Pilarski, L.M., Delovitch, T.L., and McKenzie, I.F.C. (1980). Cellular Origins of Co-stimulator (IL 2) and Its Activity in Cytotoxic T Lymphocyte Responses. J. Immunol. 124: 2231-2239.

36. Ing, P.M., Falk, J.A., Letarte, M., Delovitch, T.L. and Falk, R.E. (1979). Serological Cross-Reaction of Murine and Human Ia Antigens. Transpl. Proc. 11: 1745-1747.

37. Harris, J.R. and Delovitch, T.L. (1980). Derivation of a Monoclonal Antibody Which Detects an Ia Antigen Encoded by 2 Complementing *I*-Subregions. J. Immunol. 125: 2167-2176.

38. Delovitch, T.L., Watson, J., Battistella, R., Harris, J.F., Shaw, J., and Paetkau, V. (1981). In Vitro Analysis of Allogeneic Lymphocyte Interaction. V. Identification and Characterization of Two Components of Allogeneic Effect Factor, One of Which Displays *H-2*-Restricted Helper Activity and the Other, T Cell Growth Factor Activity. J. Exp. Med. 153: 107-128.

39. Murgita, R.A., Hooper, D.C., Stegagno, M., Delovitch, T.L., and Wigzell, H. (1981). Characterization of Murine Newborn Inhibitory T Lymphocytes: Functional and Phenotypic Comparison with an Adult T Cell Subset Activated *inVitro* by Alpha-Fetoprotein. Eur. J. Immunol. 11: 957-964.

40. Delovitch, T.L., Harris, J.F., Battistella, R., and Kaufman, K. (1982). Role of Ia Antigens in Graft-Vs.-Host Reactions. II. Molecular and Functional Analysis of T Cell Alloreactivity by the Characterization of Host Ia Antigens on Alloactivated T cells. J. Exp. Med. 155: 61-82.

41. Delovitch, T.L. and Phillips, M.L. (1982). The Biological and Biochemical Basis of Allogeneic Effect Factor (AEF) Activity: Relationship to T Cell Alloreactivity. Invited Review Article. Immunobiol. 16: 51-83.

42. Delovitch, T.L. (1983). Ia Antigens: Signals for Lymphocyte Communication. Invited Review Article. L.M. Schwartz, Ed. Compendium of Immunology 3, 2nd Edition. pp. 313-339.

43. Delovitch, T.L., Kaufman, K., and Gorczynski, R.M. (1983). *In Vitro* Analysis of Allogeneic Lymphocyte Interaction. VI. *I-J*-Restricted Self-reactive and Alloreactive Components of Allogeneic Effect Factor (AEF) are Distinct $I\text{-}J^-$ Molecules that Interact with $I\text{-}J^+$ T Cells and Antigen-Presenting Cells. J. Immunol. 130: 2241-2249.

44. Bromberg, J.S., Delovitch, T.L., Kaufman, K., and Greene, M.I. (1983). *In Vivo* Analysis of Allogeneic Lymphocyte Interaction: Activation of Suppressor T Cells by an *I-J*-Restricted Allogeneic Effect Factor (AEF). J. Immunol. 130: 2250-2255.

45. Delovitch, T.L., Kaufman, K., and Gorczynski, R.M. (1983). In Vitro Analysis of Allogeneic Lymphocyte Interaction. VII. I-*A* Restricted Self-Reactive and Alloreactive Helper Components of Allogeneic Effect Factor are Distinct Donor T Cell-Derived Ia^- Molecules that Recognize Ia Determinants on Antigen-Presenting Cells. J. Exp. Med. 157: 1794-1807.

46. Delovitch, T.L., Kaufman, K., Gorczynski, R.D., and Sinclair, G.D. (1983) *In Vitro* Analysis of Allogeneic Lymphocyte Interaction. VIII. Characterization of Helper Components of Allogeneic Effect Factor (AEF) that Activate $Lyb5^+$ and $Lyb5^-$ B Cells to Respond to Thymus Dependent and Thymus Independent Antigens. J. Immunol. 131: 2246-2253.

47. Phillips, M.L., Harris, J.F., and Delovitch, T.L. (1984). Idiotypic Analysis of Anti-I-A^k Monoclonal Antibodies. I. Production and Characterization of Syngeneic Anti-Idiotypic mAb Against an Anti-I-A^k mAb. J. Immunol. 135: 2587-2594.

48. Devaux, C.A., Phillips, M.L., and Delovitch, T.L. 1984). Idiotypic Analysis of Anti-I-A^k Monoclonal Antibodies. II. Detection of Shared Idiotopes on Syngeneic BALB/c- and Allogeneic A.TH-Derived Anti-I-A^k mAb by BALB/c-Derived Anti-I-A^k Anti-Idiotypic mAb. J. Immunol. 133: 2595-2602.

49. Sinclair, G.D., Wadgymar, A., Halloran, P.F., and Delovitch, T.L. (1984). Graft-Vs-Host Reactions Induce *H-2* Class II Gene Transcription in Host Kidney Cells. Immunogenetics 20: 503-511.

50. Jordan, B.R., Lemonnier, F.A., Le Bouteiller, P., Malissen, M., Mishal, Z., Sodoyer, R., Delovitch, T.L., Strachan, T., Damotte, M., Nguyen, C., Layet, C., Dubreuil, J., Van Agthoven, A.J., Trucy, J., and Caillol, D. (1983). Structure and Expression of Cloned HLA Class I Genes. Prog. Immunol. V: 187-201.

51. Sodoyer, R., Damotte, M., Delovitch, T.L., Trucy, J., Jordan, B.R., and Strachan, T. (1984). Complete Nucleotide Sequence of a Gene Encoding a Functional Human Class I Histocompatibility Antigen (HLA-CW3). EMB0 J. 3: 879-885.

52. Layet, C., Delovitch, T.L., Ferrier, P., Caillol, D.H., Jordan, B.R., and Lemonnier, F.A. (1985). Expression of an HLA-Bw6-Related Specificity by the HLA-Cw3 Molecule. Immunogenetics 21: 469-478.

53. Kronenberg, M., Goverman, J., Haars, R., Malissen, M., Kraig, E., Phillips, L., Delovitch, T.L., Suciu-Foca, N., and Hood, L. (1985). Rearrangement and Transcription of the ß-Chain Genes of the T Cell Antigen Receptor in Different Types of Murine Lymphocytes. Nature 313: 647-653.

54. Sinclair, G.D., Bernard, N.F., and Delovitch, T.L. (1985). Regulation of Ia Gene Transcription in Activated B cells. In: 17th Miami Winter Symposium, "Advances in Gene Technology: Molecular Biology of the Immune System". ISCU Short Reports Series. 2: 305-306.

55. Phillips, M.L. and Delovitch, T.L. (1985). Idiotypic Analysis of Anti-I-A^k Monoclonal Antibodies. III. T and B Cell Responses to Anti-Ia Idiotopes Are Not Modulated by Syngeneic Anti-Idiotypic Monoclonal Antibodies. Cell. Immunol. 96: 363-375.

56. Jordan, B.R., Caillol, D., Damotte, M., Delovitch, T., Ferrier, P., Kahn-Perles, B., Kourilsky, F., Layet C., Le Bouteiller, P., Lemonnier, F.A., Malissen, M., N'Guyen, C., Sire, J., Sodoyer, R., Strachan, T., and Trucy, J. (1985). HLA Class I Genes: From Structure to Expression, Serology and Function. Immunol. Rev. 84: 73-92.

57. Phillips, M.L., Moule, M.L., Delovitch, T.L., and Yip, C.C. (1986). Class I Histocompatibility Antigens and Insulin Receptors: Evidence for Interactions. Proc. Nat. Acad. Sci. USA 83: 3474-3478.

58. Delovitch, T.L., Phillips, M.L., Naquet, P., Yip, C.C., Lin, J., and Skinner, M. (1986). Studies on the Mechanism of Processing and Presentation of Insulin by Antigen

Presenting Cells. In: Mediators of Immune Recognition and Immunotherapy. K. Singhal and T.L. Delovitch, Eds. Elsevier Science Publishing Co. New York, NY. pp. 15-32.

59. Phillips, M.L., Yip, C.C., Shevach, E.M., and Delovitch, T.L. (1986). Photoaffinity Labeling Demonstrates Binding Between Ia Molecules and Nominal Antigen on Antigen-Presenting Cells. Proc. Nat. Acad. Sci. USA 83: 5634-5638.

60. Phillips, M.L., Naquet, P., and Delovitch, T.L. (1986). Antigen Associates with Ia Molecules In Antigen-Presenting B Cells. In: 14e Forum d'Immunologie on Antigen Processing and Presentation. Ann. Inst. Pasteur/Immunol. 137D, pp. 309-312.

61. Naquet, P., Ellis, J., Tibensky, D., Kenshole, A., Singh, B., Hodges, R., and Delovitch, T.L. (1986). Immune Response to Insulin in Type I Diabetes. In: Immunology of Diabetes Mellitus. M. Jaworski and B. Singh, Eds. Elsevier Science Publishing Co. New York. pp. 231-239.

62. Naquet, P., Ellis, J., Singh, B., Hodges, R.S., and Delovitch, T.L. (1987). Processing and Presentation of Insulin. I. Analysis of Immunogenic Peptides and Processing Requirements for Insulin A Loop-Specific T cells. J. Immunol. 139: 3955-3963.

63. Delovitch, T.L., Phillips, M.L., Naquet, P., Lin, J., Bernard, N.F., Yip, C.C., Ellis, J., and Reid, P.C. (1987). Antigen Internalization, Processing and Recycling by Antigen Presenting Cells. In: Prog. in Immunol. VI. B. Cinader and R.G. Miller, Eds. Academic Press. pp. 238.

64. Jephthah-Ochola, J., Bernard, N., Halloran, P.F., Delovitch, T.L., and Cardella, C.J. (1987). Prostacyclin Modulates Inducible Major Histocompatibility Complex Products Expression in Mouse Kidney. Transplant. Proc. 19: 216-217.

65. Bernard, N.F., Naquet, P., Watanabe, M., Hozumi, N., and Delovitch, T.L. (1988). Possible Role for Specific Surface Immunoglobulin in Antigen Presentation. In: Antigen Presenting Cells: Diversity, Differentiation and Regulation. L. Schook and J. Tew, Eds. Alan R. Liss, New York. pp. 291-300.

66. Phillips, M.L., Yip. C.C., and Delovitch, T.L. (1988). Ia-Antigen Complex Formation and Migration. In: Antigen Presenting Cells: Diversity, Differentiation and Regulation. L. Schook and J.G. Tew, Eds. Alan R. Liss, New York. pp. 311-320.

67. Naquet, P., Phillips, M.L., Ellis, J., Hodges, R., Singh, B., and Delovitch, T.L. (1988). Structural Requirements for T Cell Antigenic Sites on Insulin. In: Immunogenicity of Protein Antigens: Repertoire and Regulation. Vol. I, Chapter 2C. E. Sercarz and J. Berzofsky, Eds. CRC Uniscience Series, CRC Press Inc., Boca Raton, FL. pp. 49-56.

68. Lin, J., Berzofsky, J., and Delovitch, T.L. (1988). Ultrastructural Study of Internalization and Recycling of Antigen by Antigen Presenting Cells. J. Mol. Cell. Immunol. 3: 321-343.

69. Naquet, P., Ellis, J., Tibensky, D., Kenshole, A., Singh, B., Hodges, R., and Delovitch, T.L. (1988). T Cell Autoreactivity to Insulin in Diabetic and Related Nondiabetic Individuals. J. Immunol. 140: 2569-2578.

70. Tibensky, D., Decary, F., and Delovitch, T.L. (1988). HLA-C Genes Are Transcribed in HLA-C Blank Individuals. Immunogenetics 27: 220-224.

71. Bernard, N.F., Reid, P.C., Phillips, M.L., and Delovitch, T.L. (1988). Correlation of Presentation of Insulin with Surface I-A^d and A_α and A_β mRNA Expression by Cloned B Lymphoma Hybridoma Variants. Immunol. Letters 19: 143-152.

72. Semple, J.W., Cockle, S.A., and Delovitch, T.L. (1988). Purification and Characterization of Radiolabelled Biosynthetic Human Insulin From *Escherichia.coli*. Kinetics of Processing by Antigen Presenting Cells. Mol. Immunol. 25: 1291-1298.

73. Delovitch, T.L., Semple, J.W., and Phillips, M.L. (1988). Influence of Antigen Processing on Immune Responsiveness. Immunology Today 9: 216-218.

74. Delovitch, T.L., Semple, J.W., Naquet, P., Bernard, N.F., Ellis, J., Champagne, P., and Phillips, M.L. (1988). Pathways of Processing of Insulin by Antigen-Presenting Cells. Immunol. Rev. 106: 195-222.

75. Semple, J.W., Ellis, J., and Delovitch, T.L. (1989). Processing and Presentation of Insulin. II. Evidence for Intracellular, Plasma Membrane-Associated and Extracellular Degradation of Human Insulin by Antigen-Presenting B Cells. J. Immunol. 142: 4184-4193.

76. Stanley, J.B., Gorczynski, R.M., Delovitch, T.L., and Mills, G.B. (1989). IL-2 Secretion Is Pertussis Toxin Sensitive In a T Lymphocyte Hybridoma. J. Immunol. 142: 3546-3552.

77. Tibensky, D., DeMars, R., Holowachuk, E.W., and Delovitch, T.L. (1989). Sequence and Gene Transfer Analyses of HLA-CwBL18 (HLA-C Blank) and HLA-Cw5 Genes. Implications for the Control of Expression and Immunogenicity of HLA-C Antigens. J. Immunol. 143: 348-355.

78. Bernard, N.F., Naquet, P., Watanabe, M., Hozumi, N., and Delovitch, T.L. (1989). Influence of the Valency and Hydrophobicity of an Antigen on Its Efficiency of Processing and Presentation by Antigen-Specific B Cells. Res. Immunol. 140: 563-579.

79. Delovitch, T.L., Lazarus, A.H., Phillips, M.L., and Semple, J.W. (1989). Antigen Binding and Processing by B-Cell Antigen-Presenting Cells: Influence on T- and B-Cell Activation. In: Cold Spring Harbor Symp. Quant. Biol. LIV: 333-343.

80. Naquet, P., Ellis, J., Kenshole, A., Semple, J.W., and Delovitch, T.L. (1989). Sulfated Beef Insulin Treatment Elicits $CD8^+$ T Cells that may Abrogate Immunologic Insulin Resistance in Type I Diabetes. J. Clin. Invest. 84: 1479-1487.

81. Lazarus, A.H., Mills, G.B., and Delovitch, T.L. (1990). Antigen-Induced Ca^{2+} Signalling and Desensitization in B Cells. J. Immunol. 144: 4147-4155.

82. Christie, M.R., Daneman, D., Champagne, P., and Delovitch, T.L. (1990). Persistence of Serum Antibodies to a Reid, P.C. 64,000-*M*, Islet Cell Protein After Onset of Type I Diabetes. Diabetes 39: 653-656.

83. Christie, M.R., Vohra, G., Champagne, P., Daneman, D., and Delovitch, T.L. (1990). Distinct Antibody Specificities to a 64-kD Islet Cell Antigen in Type 1 Diabetes as Revealed by Trypsin Treatment. J. Exp. Med. 172: 789-794.

84. Tibensky, D. and Delovitch, T.L. (1990). Promoter Region of *HLA-C* Genes: Regulatory Elements Common to and Different from Those of *HLA-A* and *HLA-B* Genes. Immunogenetics 32: 210-213.

85. Semple, J.W. and Delovitch, T.L. (1991). Antigen Processing and Presentation: Functional and Molecular Aspects. In: Developmental Immunology. E.L. Cooper and E. Nisbet-Brown, Eds. Oxford Press. pp. 141.

86. Zipris,, D., Crow, A.R., and Delovitch, T.L. (1991). Does the Onset of Diabetes in NOD Mice Result From Changes in Thymic T Cell Development and Activation? In: Lessons From Animal Diabetes. III. P. Vardi and E. Shafrir, Eds. IB 16. pp. 16.1.

87. Zipris, D., Crow, A.R., and Delovitch, T.L. (1991). Altered Thymic and Peripheral T Lymphocyte Repertoire Preceding Onset of Diabetes in NOD Mice. Diabetes 40: 429-435.

88. Zipris, D., Lazarus, A.H., Crow, A.R. Hadzija, M., and Delovitch, T.L. (1991). Defective Thymic T Cell Activation by Concanavalin A and Anti-CD3 in Autoimmune Nonobese Diabetic Mice. Evidence for Thymic T Cell Anergy that Correlates with the Onset of Insulitis. J. Immunol. 146: 3763-3771.

89. Lazarus, A.H., Mills, G.B., Crow, A.R., and Delovitch, T.L. (1991). Antigen-Induced Fc Receptor-Dependent and -Independent B Cell Desensitization. An Elevation in $[CA^{2+}]_i$ is not Sufficient and Protein Kinase C Activation is not Required for These Pathways of Surface IgM-Medicated Densensitization. J. Immunol. 147: 1739-1745.

90. Wither, J., Pawling, J., Phillips, L., Delovitch, T.L., and Hozumi, N. (1991). Amino Acid Residues in the T Cell Receptor CDR3 Determine the Antigenic Reactivity Patterns of Insulin-Reactive Hybridomas. J. Immunol. 146: 3513-3522.

91. Hadzija, M., Semple, J.W., and Delovitch, T.L. (1991). Influence of Antigen Processing on Thymic T Cell Selection. Res. Immunol. 142: 421-424.

92. Semple, J.W. and Delovitch, T.L. (1991). Altered Processing of Human Insulin by B Lymphocytes from an Immunologically Insulin-Resistant Type I Diabetic Patient. Autoimmunity 4: 277-289.

93. Lazarus, A.H., Rapoport, M.J., and Delovitch, T.L. (1991). Transmembrane Signalling in the Immune System: Basic Aspects and Clinical Applications. Transplantation/Implantation Today 8: 19-22.

94. Rapoport, M.J., Zipris, D., Lazarus, A.H., Jaramillo, A., and Delovitch, T.L. (1991). Altered T Cell Development and Function in Prediabetic NOD Mice: Mechanisms and Relevance to Disease. In: HLA '91: Proceedings of 11th International Histocompatibility Conference. T. Sasazuki and S. Fuji, Eds. Oxford University Press. pp. C1.112-121.

95. Semple, J.W., Rapoport, M., and Delovitch, T.L. (1992). Immunity to Insulin. In: Insulin: Molecular Biology to Pathology. F.M. Ashcroft and S.J.H. Ashcroft, Eds. Oxford University Press. pp. 328-334.

96. Lazarus, A. H. and Delovitch, T.L. (1992). Antigen-Induced Fc Receptor-Dependent and -Independent B Cell Desensitization. In: Adv. Mol. Cell. Immunol. 1: 53-70. B. Singh, ed. JAI Press, Greenwich, CT.

97. Semple, J.W., Speck, E.R., and Delovitch, T.L. (1992). Processing and Presentation of Insulin. III. Insulin Degrading Enzyme: A Neutral Metalloendoproteinase that is Non-Homologous to Classical Endoproteinases Mediates the Processing of Insulin Epitopes for Helper T Cells. Int. Immunol. 4: 1161-1167.

98. Krook, A., Rapoport, M.J., Anderson, S., Pross, H., Zhou, Y.C., Denhardt, D.T, Delovitch, T.L., and Haliotis T. (1993). $p21^{ras}$ and Protein Kinase C Function in Distinct and Interdependent Signaling Pathways in *C3H* 10T 1/2 Fibroblasts. Mol. Cell Biol. 13: 1471-1479.

99. Forquet, F., Danilczyk, U., Lang, Y., and Delovitch, T.L. (1993). Interactions Between Peptides and MHC Molecules During Antigen Processing and Presentation. In: Chemical Immunol. "Naturally Processed Peptides". A. Sette, Ed. Karger, Basel: Switzerland. Vol. 57: pp. 63-87.

100. Rapoport, M.J., Lazarus, A.H., Jaramillo, A., Speck, E., and Delovitch, T.L. (1993). Thymic T Cell Anergy in Autoimmune Nonobese Diabetic Mice Is Mediated by Deficient T Cell Receptor Regulation of the Pathway of $p21^{ras}$ Activation. J. Exp. Med. 177: 1221-1226.

101. Christie, M.R., Hollands, J.A., Brown, T.J., and Delovitch, T.L. (1993). Detection of Pancreatic Islet 64,000 M_r Autoantigens in Insulin-Dependent Diabetes Distinct from Glutamate Decarboxylase. J. Clin. Invest. 92: 240-248.

102. Rapoport, M.J., Jaramillo, A., Zipris, D., Lazarus, A.H., Serreze, D.V., Leiter, E.H., Cyopick, P., Danska, J.S., and Delovitch, T.L. (1993). Interleukin-4 Reverses T Cell Proliferative Unresponsiveness and Prevents the Onset of Diabetes in Nonobese Diabetic Mice. J. Exp. Med. 178: 87-99.

103. Lazarus, A.H., Kawauchi, K., Rapoport, M.J., and Delovitch, T.L. (1993). Antigen-Induced B Lymphocyte Activation Involves the $p21^{ras}$ and Ras.GAP Signaling Pathway. J. Exp. Med. 178: 1765-1769.

104. Forquet, F., Hadzija, M., Semple, J.W., Speck, E., and Delovitch, T.L. (1994). Naturally Processed Heterodimeric Disulfide-Linked Insulin Peptides Bind to Major Histocompatibility Class II Molecules on Thymic Epithelial Cells. Proc. Natl. Acad. Sci. USA 91: 3936-3940.

105. Kawauchi, K., Lazarus, A.H., Rapoport, M.J., Harwood, A., Cambier, J.C., and Delovitch, T.L. (1994). Tyrosine Kinase and CD45 Tyrosine Phosphatase Activity Mediate $p21^{ras}$ Activation in B Cells Stimulated Through the Antigen Receptor. J. Immunol. 152: 3306-3316.

106. Danilczyk, U.G. and Delovitch, T.L. (1994). β_2-Microglobulin Induces a Conformational Change in an MHC Class I Chain That Occurs Intracellularly and is Maintained at the Cell Surface. J. Immunol. 153: 3533-3542.

107. Jaramillo, A., Gill, B.M., and Delovitch, T.L. (1994). Insulin Dependent Diabetes Mellitus in the Non-Obese Diabetic Mouse: A Disease Mediated by T Cell Anergy. Life Sciences 55: 1163-1177.

108. Gill, B.M., Nishikata, H., Chan, G., Delovitch, T.L., and Ochi, A. (1994). Fas Antigen and Sphingomyelin-Ceramide Turnover-Mediated Signaling: Role in Life and Death of T Lymphocytes. Immunol. Rev. 142: 113-125.

109. Delovitch, T.L., Jaramillo, A., Rapoport M.J., Laupland, K., Zipris, D., Smith, S., Kelvin, D., and Gill, B.M. (1994). Anti-Inflammatory Role of IL-4 and TH2 Cells in the Protection Against IDDM. In: Excerpta Medica International Congress Series 1100: Diabetes 1994. S. Baba and T. Kaneko, Eds. Elsevier Science Publishers, Amsterdam, The Netherlands. pp. 203-209.

110. Gill, B.M., Jaramillo, A., Ma, L., Laupland, K.B., and Delovitch, T.L. (1995). Genetic Linkage of Thymic T-Cell Proliferative Unresponsiveness to Mouse Chromosome 11 in NOD Mice: A Possible Role for Chemokine Genes. Diabetes 44: 614-619.

111. Cameron, M.J., Arreaza, G.A., and Delovitch, T.L. (1995). Interleukin-4. Diabetes Dialogue 42: 18-19.

112. Arreaza, G.A., Cameron, M.J., and Delovitch, T.L. (1996). Interleukin-4: Potential Immunoregulatory Agent in Therapy of Insulin-Dependent Diabetes. Clin. Immunother. 6: 251-260.

113. Kawauchi, K., Lazarus, A.H., Sanghera, J.S., Leung Pui Pan, G., Pelech, S.L., and Delovitch, T.L. (1996). Regulation of BCR- and PKC/Ca^{2+}-Mediated Activation of the Raf-1/MEK/MAPK Pathway by Protein-Tyrosine Kinase and -Tyrosine Phosphatase Activities. Mol. Immunol. 33: 287-296.

114. Lang, Y., Forquet, F., Speck, E., Blum, J., and Delovitch, T.L. (1996). Major Histocompatibility Complex Class II Molecules Function As a Template for the

Processing of a Partially Processed Insulin Peptide into a T Cell Epitope. Diabetes 45: 1711-1719.

115. Beales, P.E., Delovitch, T.L., Signore, A., and Pozzili, P. (1996). Standardizing Experiments with NOD Mice. Autoimmunity 24: 127-129.

116. Brownell, H.L., Firth, K.L., Kawauchi, K., Delovitch, T.L., and Raptis, L. (1997). A Novel Technique for the Study of Ras Activity: Electroporation of [α^{32}P]GTP. DNA and Cell Biol. 16: 103-110.

117. Salojin, K., Zhang, J., Cameron, M., Gill, B., Arreaza, G., Ochi, A., and Delovitch, T.L. (1997). Impaired Plasma Membrane Targeting of Grb2-Murine Son of Sevenless (mSOS) Complex and Differential Activation of the Fyn-T Cell Receptor (TCR)-ζ-Cbl Pathway Mediate T Cell Hyporesponsiveness in Autoimmune Nonobese Diabetic Mice. J. Exp. Med. 186: 887-897.

118. Arreaza, G.A., Cameron, M.J., Jaramillo, A., Gill, B.M., Hardy, D., Laupland, K.B., Rapoport, M.J., Zucker, P., Chakrabarti, S., Chensue, S.W., Qin, H.-Y., Singh, B., and Delovitch, T.L. (1997). Neonatal Activation of CD28 Signaling Overcomes T Cell Anergy and Prevents Autoimmune Diabetes by an IL-4 Dependent Mechanism. J. Clin. Invest. 100: 2243-2253.

119. Cameron, M.J., Arreaza, G., and Delovitch, T.L. (1997). IL-4 Prevents Insulitis and Insulin-Dependent Diabetes Mellitus in Nonobese Diabetic Mice by Potentiation of Regulatory T Helper-2 Cell Function. J. Immunol. 159: 4686-4692.

120. Bergerot, I., Arreaza, G.A., Cameron, M.J., Chou, B., and Delovitch T.L. (1997). Role of T Cell Anergy and Suppression in Susceptibility to IDDM. Forum on "The NOD Mouse", D. Mathis and J.F. Bach, Eds. Res. Immunol. 148: 348-358.

121. Cameron, M.J., Arreaza, G.A., and Delovitch T.L. (1997). Cytokine- and Costimulation-Mediated Therapy of IDDM. Crit. Rev. Immunol. 17: 537-544.

122. Fantus, I.G., Delovitch, T.L., and Dupré, J. (1997). Prevention of Diabetes Mellitus: Goal for the Twenty-First Century: Part Two. Can. J. Diab. Care 21: 14-22.

123. Delovitch, T.L. and Singh, B. (1997). The Nonobese Diabetic Mouse As a Model of Autoimmune Diabetes: Immune Dysregulation Gets the NOD. Immunity 7: 727-738.

124. Zhang, J., Salojin, K., and Delovitch, TL. (1998). Sequestration of CD4-Associated Lck from the TCR Complex May Elicit T Cell Hyporesponsiveness in Nonobese Diabetic Mice. J. Immunol. 160: 1148-1157.

125. Cameron, M.J., Meagher, C., and Delovitch, T.L. (1998). Failure in Immune Regulation Begets IDDM in NOD Mice. Diabetes/Metabolism Rev. 14: 177-185.

126. Zhang, J., Salojin, K., Gao J.-X., Cameron, M., Geisler, C., and Delovitch, T.L. (1998). TCRαβ Chains Associate with the Plasma Membrane Independently of CD3 and TCRζ Chains in Murine Primary T Cells. J. Immunol. 161: 2930-2937.

127. Salojin, K., Zhang, J., Madrenas, J., and Delovitch, T.L. (1998). T-Cell Anergy and Altered T-Cell Receptor Signaling: Effects on Autoimmmune Disease. Immunol. Today 19: 468-473.

128. Arreaza, G.A., Bergerot, I., Cameron, M.J., Salojin, K., Zhang, J., Tung, H., and Delovitch, T.L. (1998). Immune Dysregulation Elicits Type I Diabetes Mellitus in NOD Mice. Can. J. Diab. Care 22: S20-S23.

129. Hill, D., Petrik, J., Arany, E., McDonald, T.J., and Delovitch, T.L. (1999). Insulin-Like Growth Factors Prevent Cytokine-Mediated Cell Death In Isolated Islets of Langerhans from Pre-Diabetic Non-Obese Diabetic Mice. J. Endocrinol. 161: 153-165.

130. Arreaza, G.A., Bergerot, I., Cameron, M.J., Salojin, K., Zhang, J., Tung, H., Meagher, C., and Delovitch, T.L. (1999). Immune Modulation in Prevention of Type I Diabetes. Can. J. Diab. Care 23: 33-39.

131. Zhang, J., Salojin, K.V., Gao, J.-X., Cameron, M., Bergerot, I., and Delovitch, T.L. (1999). p38 Mitogen-Activated Protein Kinase Mediates Signal Integration of TCR/CD28 Costimulation in Primary Murine T Cells. J. Immunol. 162: 3819-3829.

132. Salojin, KV., Zhang, J., and Delovitch, T.L. (1999). TCR and CD28 Are Coupled Via ZAP-70 to the Activation of the Vav/Rac-1/PAK-1/p38 MAPK Signaling Pathway. J. Immunol. 163: 844-853.

133. Bergerot, I., Arreaza, G.A, Cameron, M.J., Burdick, M.D., Strieter, R.M., Chensue, S.W., Chakrabarti, S., and Delovitch, T.L. (1999). Insulin B-Chain Reactive $CD4^+$ Regulatory T Cells Induced by Oral Insulin Treatment Protect from Type 1 Diabetes by Blocking the Cytokine Secretion and Pancreatic Infiltration of Diabetogenic Effector T Cells. Diabetes 48: 1720-1729.

134. Salojin, K.V., Zhang, J., Meagher, C., and Delovitch, T.L. (2000). ZAP-70 Is Essential for the T Cell Antigen Receptor-induced Plasma Plasma Membrane Targeting of SOS and Vav in T Cells. J. Biol. Chem. 275: 5966-5975.

135. Zhang, J., Gao, J.-X., Salojin, K.V., Shao, Q., Grattan, M., Meagher, C., Laird, D., and Delovitch, T.L. (2000). Regulation of Fas Ligand Expression During Activation-Induced Cell Death in T Cells by p38 Mitogen-Activated Protein Kinase and c-Jun NH_2-Terminal Kinase. J. Exp. Med. 191: 1017-1030.

136. Gao, J.-X., Zhang, J., Awaraji, C., Bhatia, M., Jevnikar, A., Singh, B., Bell, D., and Delovitch, T.L. (2000). Preferential Proliferation and Differentiation of Double Positive Thymocytes Into $CD8^+$ Single Positive Thymocytes in a Novel Cell Culture Medium. Cell. Immunol. 202: 41-53.

137. Cameron, M.J., Arreaza, G.A., Grattan, M.A., Meagher, C., Sharif, S., Burdick, M.D., Strieter, R.M., Cook, D., and Delovitch, T.L. (2000). Differential Expression of CC Chemokines and the CCR5 Receptor in the Pancreas Is Associated with Progression of Type 1 Diabetes. J. Immunol. 165: 1102-1110.

138. Cameron, M.J., Strathdee, C.A., Holmes, K.D., Arreaza, G.A., Dekaban, G.A., and Delovitch, T.L. (2000). Biolistic-Mediated Interleukin-4 Gene Transfer Prevents the Onset of Type 1 Diabetes. Human Gene Therapy 11: 1647-1656.

139. Cameron, M.J., Arreaza, G.A., Waldhauser, L., Gauldie, J., and Delovitch, T.L. (2000). Immunotherapy of Spontaneous Type 1 Diabetes in Nonobese Diabetic Mice by Systemic Interleukin-4 Treatment Employing Adenovirus Vector-Mediated Gene Transfer. Gene Ther. 7: 1840-1846.

140. Singh, B. and Delovitch, T.L. (2000). Immune Mechanisms that Regulate Susceptibility to Autoimmune Type I Diabetes. Clin. Rev. Aller. Immunol. 19: 247-264.

141. Zhang, J., Salojin, K.V., Arreaza, G.A., Cameron, M.J., and Delovitch, T.L. (2001). CD28 Costimulation Restores Normal TCR-Mediated Transcriptional Regulation of IL-2 and IL-4 Genes in T Cells from Nonobese Diabetic Mice. Int. Immunol. 13: 377-384.

142. Sharif, S., and Delovitch, T.L. (2001). Regulation of Immune Responses by Natural Killer T (NKT) Cells. Special Issue on Innate Immunity. Arch. Immunol. Ther. Exp. 49 Suppl 1: S23-S31.

143. Arreaza, G.A., Sharif, S., Cameron, M.J., Chen, W., and Delovitch, T.L. (2001). Role of Regulatory T Cells in the Pathogenesis of Type 1 Diabetes. Curr. Dir. Autoimmun. 4: 308-332.

144. Meagher, C., Sharif, S., Hussain, S., Cameron, M.J., Arreaza, G.A., and Delovitch, T.L. (2002). Role of Cytokines and Chemokines in Autoimmune Type 1 Diabetes. In: "Cytokines in Autoimmune Disease". P. Santamaria, Ed. Landes Bioscience. In Press.

145. Sharif, S.; Arreaza, G.A.; Zucker, P.; and Delovitch, T.L. (2002). Regulatory NKT cells protect against spontaneous and recurrent type 1 diabetes. In: Immunology of Diabetes: Autoimmune Mechanisms and the Prevention and Cure of Type 1 Diabetes. C.B. Sanjeevi, Ed. Ann. N.Y. Acad. Sci. 958: 77-88.

146. Chen, W., Bergerot, I., Elliot, J.F., Harrison, L.C., Abiru, N., Eisenbarth, G., and Delovitch, T.L. (2001). Evidence that a Peptide Spanning the B-C Junction of Proinsulin is a Primary Autoantigen Epitope in the Pathogenesis of Type 1 Diabetes. J. Immunol. 167: 4926-4935.

147. Sharif, S., Arreaza, G.A., Zucker, P., Mi, Q-S, Sondhi, J., Naidenko, O.V., Kronenberg, M., Koezuka Y., and Delovitch, T.L.; Gombert, J.M., Leite-de-Moraes, M., Gouarin, C., Zhu R., Hameg, A., Nakayama, T., Taniguchi, M., Lepault, F., Lehuen, A., Bach, J.F. and Herbelin, J.F. (2001). Activation of NKT Cells by Alpha Galactosylceramide Treatment Prevents the Onset and Recurrence of Autoimmune Type I Diabetes. Nature Med. 7: 1057-1062. **[Highlighted in Nat. Rev. Immunol. 1: 4 (2001) and Trends in Immunol. 22; 597 (2001)]**

148. Grattan, M., Mi, Q.-S., Meagher, C., and Delovitch, T.L. (2002). Congenic Mapping of the Diabetogenic Locus *Idd4* to a 5.2 cM Region of Chromosome 11 in NOD Mice: Identification of Two Candidate Subloci. Diabetes 51: 215-223.

149. Sharif S., Arreaza, G.A., G.A., Zucker, P., Mi, Q-S, and Delovitch, T.L. (2002). Regulation of Autoimmune Disease by NKT Cells. J. Mol. Med. 80: 290-300.

150. Mi, Q-S, Meagher, C., and Delovitch, T.L. (2002). CD1d Restricted NKT Regulatory Cells: Functional Genomic Analyses Provide New Insight into Mechanism of Protection from Type 1 Diabetes. Novartis Foundation Symposium 252 on "Generation and Effector Functions of Regulatory Lymphocytes", In press.

151. Delovitch, T.L., and Wilson, B.W. (2002). CD1d-restricted NKT cells: Functional regulation by close encounters with dendritic cells. Nature Rev. Immunol., In press.

Refereed Papers, Submitted/In Preparation

1. Mi, Q-S,. Sivilotti M., Zhou L., and Delovitch, T.L. (2002). Evidence that *PAF-AH Ib1* may not be a Candidate Gene of the *Idd4.1* Diabetes-Susceptibility Locus in NOD Mice. Diabetes, Submitted.

2. Arreaza, G., Salojin, K., Yang, W., Zhang, J., Gill, B., Gao, J.-X., Meagher, C., Cameron, M., and. Delovitch, T.L. (2002). Resistance of T Cells to T Cell Receptor Activation Induced Apoptosis in Nonobese Diabetic Mice. Possible Role in the Pathogenesis of Type 1 Diabetes. J. Immunol. (Under Re-review).

3. Hussain S, Salojin, K.V., Zucker, P., and Delovitch, T. L. (2002). Hyperresponsiveness, Increased Cell Division and Resistance to Apoptosis of Activated Autoreactive B Cells May Mediate Their Survival and Migration into Inflamed Islets in Nonobese Diabetic Mice. J. Immunol., Submitted.

4. Mi, Q-S., Ly, D., Lamhamedi-Cherradi, S-E, Salojin, K. V., Zhou, L., Grattan, M., Meagher, C., Zucker, P., Chen, Y. H., Nagle, J., Taub, D., and Delovitch, T. L. (2002). Blockade of TNF-Related Apoptosis-Inducing Ligand (TRAIL) Exacerbates Autoimmune Type 1 Diabetes in NOD Mice. J. Clin. Invest., Submitted.

5. Meagher, T. C., Mi, Q-S., Cruikshank, W. W., Arreaza, G. A., Chen, W., and Delovitch, T. L. (2002). IL-16 Plays an Inflammatory Role in the Development of Insulitis and Type 1 Diabetes. In preparation.

ABSTRACTS (1995-2002)

5. Gill BM and Delovitch TL. 1995. Increased T cell programmed cell death (PCD) may predispose to insulin-dependent diabetes mellitus (IDDM). Keystone Symposium on "Apoptosis". Mar. 5-11. Tamarron, CO.
6. Gill BM, and Delovitch TL. 1995. Elevated T cell PCD susceptibility may mediate onset of insulin-dependent diabetes mellitus. 9th International Congress of Immunology. July 23-29. San Francisco, CA.
7. Salojin K, Gill BM, and Delovitch TL. 1995. NOD thymocyte unresponsiveness is mediated by TCR/CD4 dependent tyrosine hyperphosphorylation. Symposium on "Immunological Tolerance". Oct. 22-24. London, Ontario.
8. Zhang J, and Delovitch TL. 1995. Hyperactivation of Lck may uncouple the TCR and mediate the proliferative unresponsiveness of NOD thymocytes. Symposium on "Immunological Tolerance". Oct. 22-24. London, Ontario.
9. Arreaza G, Cameron MJ, and Delovitch TL. 1995. Role of IL-4 in the pathogenesis of IDDM. Symposium on "Immunological Tolerance". Oct. 22-24. London, Ontario.
10. Hill DJ, and Delovitch TL. 1995. Insulin-like growth factors protect isolated islets of Langerhans from the cytotoxic effects of cytokines. 186th Meeting of the Society for Endocrinology. Nov. 22-23. London, U.K.
11. Horrocks C, Gill BM, and Delovitch TL. 1995. Possible role of APC dysfunction in TCR-mediated T cell unresponsiveness and apoptosis in NOD mice. Workshop on "Antigen Processing and Presentation". Nov. 30-Dec. 3. Oxnard, CA.
12. Cameron M, Arreaza G, and Delovitch TL. 1996. Mechanism of IL-4-mediated protection from IDDM in NOD mice. Tenth Canadian Soc. for Immunol. Meeting. Mar. 22-25. Mont Rolland, Quebec.
13. Arreaza G, Cameron M, and Delovitch TL. 1996. Effects of IL-4 administration and CD28 costimulation in the pathogenesis of IDDM in NOD mice. Keystone Symposium on "Lymphocyte Activation". Mar. 20-26. Hilton Head, SC.
14. Zhang J, and Delovitch TL. 1996. Hyper-activation of Lck may uncouple the TCR and mediate the proliferative unresponsiveness of NOD thymocytes. Keystone Symposium on "Lymphocyte Activation". Mar. 20-26. Hilton Head, SC.
15. Salojin K, Gill BM, and Delovitch TL. 1996. NOD thymocyte anergy is mediated by TCR/CD4-dependent tyrosine hyperphosphorylation. Keystone Symp. on "Signal Transduction Tyrosine Kinases". Mar. 27-Apr. 2. Taos, NM.
16. Cameron MJ, Arreaza GA, and Delovitch TL. 1996. Mechanisms of protection by IL-4 in the pathogenesis of IDDM in the NOD mouse. First Annual Maragaret P. Moffat Graduate Research Day Symposium, Faculty of Medicine, UWO. May 7. London, ON.
17. Chou H, and Delovitch TL. 1996. Isolation and characterization of insulin B chain specific Th2 cells that protect NOD mice from IDDM. First Annual Maragaret P. Moffat Graduate Research Day Symposium, Faculty of Medicine, UWO. May 7. London, ON.
18. Delovitch TL. 1996. Novel approaches to IDDM therapy: cytokine and oral antigen administration. Banting and Best Diabetes Center (BBDC) Scientific Day. May 10. Toronto, ON.
19. Gill B, Horrocks C, and Delovitch TL. 1996. T cell-APC interactions in NOD mice. American Association of Immunologists Meeting. June 2-6. New Orleans, LA.
20. Bergerot I, and Delovitch TL. 1996. Oral insulin administration restores Deficient T suppressor cell function may mediate the onset of IDDM in NOD mice and may be restored by oral insulin administration. 75th Anniversary Symposium of the Discovery of Insulin. Oct. 6-9. Toronto, ON.

21. Cameron MJ, Arreaza GA, Chakrabarti S, and Delovitch TL. 1996. IL-4 administration and CD28 costimulation potentiates regulatory Th2 cell function and prevent IDDM in NOD mice. 75th Anniversary Symposium of the Discovery of Insulin. Oct. 6-9. Toronto, ON.
22. Zhang J., Salojin K., and Delovitch TL. 1996. Hyper-activation of Lck may uncouple the TCR and mediate the proliferative unresponsiveness of NOD thymocytes. 75th Anniversary Symposium of the Discovery of Insulin. Oct. 6-9. Toronto, ON.
23. Hill DJ, and Delovitch TL. 1996. Protection of isolated islets from prediabetic NOD mice against cytokine-induced cell death by insulin-like growth factors. 75th Anniversary Symposium of the Discovery of Insulin. Oct. 6-9. Toronto, ON.
24. Arreaza GA, Cameron MJ, Chakrabarti S, and Delovitch TL. 1997. CD28 costimulation prevents insulin dependent diabetes by an IL-4 dependent mechanism in NOD mice. AAAAI/AAI/CIS Joint Meeting. Feb. 21-26. San Francisco, CA.
25. Delovitch TL, Salojin K, Zhang J, Cameron M, Gill B, Arreaza G, and Ochi A. 1997. Tyrosine hyperphosphorylation of the TCR/CD3 complex and deficient ras GDP releasing factor (GRF) activity mediate T cell anergy in autoimmune nonobese diabetic mice. Canadian Society for Immunology. Mar. 14-17. Lake Louise, AB.
26. Zhang J, Salojin K, Ball E, Delovitch TL. 1997. Sequestration of CD4-associated Lck from the TCR/CD3 complex elicits a deficient coupling of TCR-mediated signaling and may mediate NOD T cell anergy. Canadian Society for Immunology. Mar. 14-17. Lake Louise, AB.
27. Cameron MJ, Arreaza GA, Chakrabarti S, Strieter RW, and Delovitch TL. 1997. Early IL-4 treatment prevents insulitis and IDDM in NOD mice via potentiation of Th2 cell function and modulation of lymphocyte migration. Keystone Symposium on "Tolerance and Autoimmunity". Apr. 13-19. Keystone, CO.
28. Delovitch TL. 1996. Immunogenetics, Immunopathogenesis and Immunotherapy of IDDM. 75th Anniversary Symposium of the Discovery of Insulin. Oct. 6-9. Toronto, ON.
29. Bergerot I, Chakrabarti S, and Delovitch TL. 1997. Oral insulin administration restores deficient T suppressor cell function in NOD mice. Keystone Symposium on "Tolerance and Autoimmunity". Apr. 13-19. Keystone, CO.
30. Salojin K, Zhang J, Cameron M, Gill B, Arreaza G, Ochi A, and Delovitch TL. 1997. Tyrosine hyperphosphorylation of the TCR/CD3 complex and deficient Ras GDP releasing factor (GRF) activity mediate T cell anergy in autoimmune nonobese diabetic mice. Keystone Symposium on "Tolerance and Autoimmunity". Apr. 13-19. Keystone, CO.
31. Delovitch TL, Cameron MC, and Arreaza GA. 1997. Cytokine- and costimulation-mediated prevention of autoimmune diabetes. Ninth Annual Symposium on Immunobiology of Proteins and Peptides. Invited Symposium Talk. May 20-24. Whistler, BC
32. Delovitch TL, Cameron MC, and Arreaza GA. 1997. Cytokine- and costimulation-mediated prevention of autoimmune diabetes. FASEB Summer Conference on "Autoimmunity". Invited Symposium Talk. June 21-26. Saxton's River, VT.
33. Delovitch TL et al. 1997. Workshop on "Regulation of Autoimmunity: Diabetes, EAE/MS, and Arthritis". Talks on "Prevention of IDDM by treatment with IL-4 and Anti-CD28", and "Tyrosine hyperphosphorylation of the TCR/CD3 Complex and deficient Ras GDP releasing factor activity mediate T cell unresponsiveness in NOD mice". Sept. 17-20. Genoa, Italy.

34. Delovitch TL. 1997. Immune Dysregulation as a Susceptibility Factor in Type I Diabetes. First Annual Canadian Diabetes Association Conference. Invited Symposium Talk. October 23-25. London, ON.
35. Delovitch TL. 1998. Novel Approaches to Immunotherapy of Type I Diabetes in the 21st Century. Toronto Diabetes Society Symposium on Prevention of Type I Diabetes. Invited Symposium Talk. May 13. Toronto, ON
36. Salojin KV, Zhang J, and Delovitch TL. 1998. Differential activation of SOS-Grb-2 and Vav-Rac-1 mediated signaling in TCR- and CD28-stimulated T cells. American Association of Immunology meeting. April 14-20. San Francisco, CA.
37. Gao JX, Zhang J, Bergerot I, Bell D, and Delovitch TL. 1998. Regulation of thymocyte differentiation by IL-4. Keystone Symposium on "Tolerance and Autoimmunity". Jan. 26-Feb. 1. Keystone, CO.
38. Zhang J, Salojin KV, Gao JX, Cameron M, and Delovitch TL. 1998. p38MAPK is involved in both TCR and CD28-mediated signaling pathways in primary murine T cells. Keystone Symposium on "Tolerance and Autoimmunity". Jan. 26-Feb. 1. Keystone, CO.
39. Cameron MJ, Arreaza GA, and Delovitch TL. 1998. Modulation of intra-islet chemokines by CD28 costimulation in vivo. 3rd Immunology of Diabetes Society Congress. June 20-23. Chicago, IL.
40. Cameron MJ, Holmes KD, Delovitch TL, Strathdee CA, and Dekaban GA. 1998 Early biolistic delivery of an IL-4 expression vector prevents insulitis and IDDM in NOD mice. American Society of Gene Therapy meeting. June 19-24. San Francisco, CA.
41. Cameron MJ, Arreaza GA, Holmes KD, Strathdee CA, and Dekaban GA, and Delovitch TL. 1998. Early biolistic delivery of an IL-4 expression vector prevents insulitis and IDDM in NOD mice. American Diabetes Association meeting. June 24-26. Chicago, IL.
42. Cameron MJ, Arreaza GA, Grattan MA, and Delovitch TL. 1999. IL-4 treatment modulates the role of MIP-1α in the pathogenesis of autoimmune diabetes. Keystone Symposium on "Tolerance and Autoimmunity". Mar. 26-Apr. 1. Keystone, CO
43. Gao JX, Zhang J, Bell D, Delovitch TL. 1999. XLCM™ reverses the pathogenicity of autoreactive T cells and prevents the adoptive transfer of IDDM. Worcester Translational Research Conference on "Bone Marrow Transplantation for the Treatment of Autoimmune Disease". Sept. 24-25. Worcester, MA.
44. Cameron MJ, Arreaza GA, Grattan MA, Meagher C, Burdick MD, Strieter RM, Cook DN, Smithies O, and Delovitch TL. 1999. Differential intra-pancreatic expression of CC chemokines mediates the pathogenesis of type I diabetes. 4th Immunology of Diabetes Society Congress. Nov. 13-15. Fiuggi, Rome.
45. Arreaza GA, Salojin K, Zhang J, Cameron MJ, and Delovitch TL. 2000. Role of T cell resistance to activation induced cell death (AICD) in susceptibility to autoimmune diabetes. American Association of Immunologists. "Immunology 2000" Meeting. May 12-16. Seattle, WA.
46. Cameron JM, Arreaza G, Holmes KD, Strathdee CA, Dekaban GA, and Delovitch TL. 2000. Immunotherapy of spontaneous type 1 diabetes in NOD mice by systemic interleukin-4 treatment employing biolistic plasmid DNA and adenovirus vector-mediated gene transfer. American Association of Immunologists. "Immunology 2000" meeting. May 12-16. Seattle, WA.
47. Salojin KV, Arreaza G, Gill B, Zhang J, and Delovitch TL. 2000. Role of T cell resistance to activation-induced cell death (AICD) in susceptibility to type 1 diabetes.

First Juvenile Diabetes Foundation International Workshop for Fellows and Career Award Recipients.

48. Chen W, Bergerot I, Elliott J, and Delovitch. 2000. Lack of Neonatal tolerance to proinsulin elicits the pathogenesis IDDM in NOD mice. 2000. Keystone Symposium on "Mechanisms of Immunologic Tolerance and Its Breakdown". March 31-April 6. Steamboat Springs, CO.
49. Sharif, S, Arreaza GA, and Delovitch, TL. 2000. Alpha-galactosylceramide (AGC) prevents development and accelerated diabetes in the NOD mouse model. Keystone Symposium on "Mechanisms of Immunologic Tolerance and Its Breakdown". March 31-April 6. Steamboat Springs, CO.
50. Sharif, S, and Delovitch, T.L. 2001. Regulatory NKT cells protect against spontaneous and recurrent Type I Diabetes. 5th International Congress of the Immunology of Diabetes Society. February 14-16. Chennai (Madras) India.
51. Meagher, T.C.; Arreaza, G.; Cameron, M.; Delovitch, T.L. 2001. The Role of MIP-1α and MIP-1β In Adoptive Transfer Models of Type 1 Diabetes. Annual Meetings of Federation of Societies for Experimental Biology (FASEB). March 31-April 1, 2001. Orlando, FL.
52. Salojin, K, Arreaza, GA, and Delovitch, TL. 2001. Role of T cell resistance to activation-induced cell death (AICD) in susceptibility to autoimmune type 1 diabetes. 11th International Congress of Immunology. July 22-27. Stockholm, Sweden.
53. Cameron, MJ, Strathdee, C, Holmes, KD, Arreaza, GA, Dekaban GA, Sharif, S, Zucker, P, Mi, Q-S, Sondhi, J, Naidenko, O, Kronenberg, M, Koezuka, Y, and Delovitch, TL. 2001. Prevention of type 1 diabetes by both biolistic-mediated interleukin-4 gene transfer and activation of NKT cells by treatment with alpha-galactosylceramide. International Conference on "Emerging Technologies in Gene/Drug Therapy and Molecular Biology". Aug. 25-31. Corfu, Greece.
54. Mi, Q.-S., Meagher, C., Nagel, J, Zucker, P, Taub, DD, and Delovitch, TL. 2002. Gene expression profiling of pancreatic islets during the pathogenesis of type 1 diabetes in NOD mice. Annual Meeting of Federation of Societies for Experimental Biology (FASEB) on "Translating the Genome". Apr. 20-24. New Orleans, LA.
55. Chen, W, Salojin, K, Zucker, P, and Delovitch, TL. 2002. Treatment of NOD mice with an IGF-I/IGFBP3 complex protects against type 1 diabetes. Annual Meeting of Federation of Societies for Experimental Biology (FASEB) on "Translating the Genome". Apr. 20-24. New Orleans, LA.
56. Hussain, S, Salojin, K, and Delovitch, TL. 2002. Phenotypic and functional characterization of B cells from nonobese diabetic (NOD) mice. Canadian Society for Immunology. April 5-8. Blue Mountain Resort, Collingwood, ON.
57. Meagher, TC, Mi, Q-S, Cruikshank, W.W., Arreaza, G., Chen, W, and Delovitch, TL. 2002. IL-16 plays an inflammatory role in the development of insulitis and type 1 diabetes. Federation of Clinical Immunology Societies (FOCIS) Second Annual Meeting. June 27-30. San Francisco, CA.
58. Mi, Q-S, Meagher, TC.; and Delovitch, TL. 2002. Regulation of susceptibility to type 1 diabetes by NKT cells. Novartis Foundation Symposium on "Generation and Effector Functions of Regulatory Lymphocytes". July 9-11. London, U.K.
59. Meagher, TC, Mi, Q-S, and Delovitch, TL. 2002. Counter-regulatory roles of IL-16 and MIP-1β in the pathogenesis of type 1 diabetes. 6th International Congress of Immunology of Diabetes Society. October 3-6. Copper Mountain, CO.
60. Delovitch, TL. 2002. NKT regulatory cells: functional genomic analyses provide new insights into their mechanism of protection against Type 1 diabetes. CD1 and NKT Cell Workshop. Nov. 5-8. Woods Hole, MA.

61. Delovitch, TL. 2003. Protection against type 1 diabetes by regulation of NKT cells, IL-16 and CCL4 activity. Keystone Symposium on "Mechanisms of Immunologic Tolerance and its Breakdown. Jan. 7-13. Snowbird, Utah.

References

1. Tesfaye S, Malik R, Ward JD (1994) Vascular factors in diabetic neuropathy Diabetologia 37: 847–854
2. Simpson LO (1994) Essential fatty acid treatment of rats with experimental diabetes: comment. Diabetologia 37 331
3. Simpson LO (1989) Blood from healthy animals and humans contains nondiscocytic erythrocytes. Br J Haematol 73: 561–564
4. Vracko R (1974) Basal lamina layering in diabetes Evidence for accelerated rate of cell death and cell regeneration. Diabetes 23: 94–104
5. Schoefl GI (1964) Electron microscopic observations on the regeneration of blood vessels after injury Ann NY Acad Sci 116: 789–802
6. Jamal GA, Carmichael H (1990) The effect of gammalinolenic acid on human diabetic peripheral neuropathy: a double-blind placebo controlled trial. Diabet Med 7: 319–323
7. Cameron NE, Cotter MA, Robertson S (1991) Essential fatty acid diet supplementation: effects on peripheral nerve and skeletal muscle function and capillarisation in streptozotocin-induced diabetic rats. Diabetes 40: 532–539
8. Kury PG, Ramwell PW, McConnell HM (1974) The effect of prostaglandins E_1 and E_2 on the human erythrocyte as monitored by spin labels. Biochim Biophys Res Commun 56: 478–483
9. Rassmussen H, Lake W, Allen JE (1975) The effect of catecholamines and prostaglandins upon human and rat erythrocytes. Biochim Biophys Acta 411: 63–73
10. Horrobin DF (1992) Nutritional and medical importance of gammalinolenic acid Progr Lipid Res 31: 163–194
11. Simpson LO (1991) Red cell shape in different anticoagulants. Br J Haematol 79: 136–137 (Letter)
12. Simpson LO (1993) The effects of saline solutions on red cell shape: a scanning electron microscope based study. Br J Haematol 85: 832–834

Response from the authors

Dear Sir,

We are most interested in the comments of Dr. L.O. Simpson regarding the importance of intracapillary blood constituents and endothelial cells in the damaging effects of capillary disease in diabetic nerve. We would agree with the opinion that this is probably just as important as the abnormal haemodynamics in the vessels supplying the nerve. In the original studies of sural nerve biopsies where capillary endothelial changes were noted [1–3] many of the vessels showed debris which was undoubtedly of cellular nature with fibrin and in some instances small plugs of deactivated platelets. However, we would agree that the haemodynamic factors within the nerve are extremely difficult to assess in vivo. We would suggest that there is an urgent need for relatively non-invasive methods of measuring nerve blood flow, perhaps as simple as nerve oxygen tension to study the varying effects of the metabolic state and the influence of drugs known to affect nerve blood flow in animals.

Yours sincerely,
S Tesfaye, R Malik, J D Ward

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References

1. Timperly WR, Ward JD, Preston FE, Duckworth T, O'Malley BC (1976) Clinical and histological studies in diabetic neuropathy. Diabetologia 12: 237–243
2. Williams E, Timperly WR, Ward JD, Duckworth T (1980) Electronmicroscopical studies of vessels in diabetic peripheral neuropathy. J Clin Pathol 33: 462–470
3. Timperly WR, Boulton AJM, Davies Jones GAB, Jarrat JA, Ward JD (1985) Small vessel disease in progressive diabetic neuropathy associated with good metabolic control J Clin Pathol 38: 1030–1038

The cumulative incidence of childhood diabetes mellitus in Sweden unaffected by BCG-vaccination

Dear Sir,

Several studies in the diabetes-prone nonobese diabetic (NOD) mouse have shown that even one single injection of either complete Freund's adjuvant (CFA) [1] or BCG-vaccine [2] given at an early age prevented the development of diabetes in this animal model. The mechanism has been indicated to be due to a non-specific stimulation of natural suppressor activity. Recently, Shehadeh et al [3] reported that CFA and BCG vaccine modulated the development of diabetes mellitus in NOD mice. Furthermore in an open clinical trial in 17 newly-diagnosed insulin-dependent diabetes mellitus (IDDM) patients intracutaneous administration of 0.1 ml BCG-vaccine (1 mg/ml) led to a clinical remission more frequently when compared to non-treated control subjects. Based on these indications several large-scale placebo-controlled trials have been started in diabetic humans including children with primary prevention in healthy children as a goal.

In Sweden, since 1 July 1977 we have continuously registered all childhood-onset diabetic cases with a level of ascertainment close to 99% [4]. Before 1975 all newborn babies in Sweden were offered BCG-vaccination (using the dose given above) in the first month of life and the coverage of this vaccination programme was almost complete [5, 6]. Due to side effects, in some cases severe complications, this policy was stopped on 1 April 1975. Since then only high-risk groups such as immigrant children or children with a close relative with tuberculosis have been vaccinated. In 1976 only 0.6% were vaccinated [5] and between 1976–1980 less than 2% were vacci-

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nated [6]. When comparing cumulative incidence rates of IDDM up to 15 years of age between birth cohorts 1973, 1974 and 1976, 1977 (Fig. 1) there is clearly no significant difference. As can be seen, the cumulative incidence was slightly lower during 1974 whereas 1973, 1976 and 1977 are almost identical. Since the incidence registration of childhood diabetes started on 1 July 1977 cumulative incidence rates in children with disease onset before the age of 4 years could not be compared. The proportion of diabetic patients in these age-groups is, however, very low, between 10–15% (e.g. 46/367 in 1977). An effect of BCG vaccination on the incidence of IDDM in very young-onset diabetic patients thus could not be excluded but would not account for a large proportion of cases.

We conclude that, on a population basis, BCG-vaccination in newborn children seems to have no significant effect on the incidence of childhood-onset IDDM and therefore would not offer an effective primary prevention strategy.

Sincerely yours,
G. Dahlquist, L. Gothefors

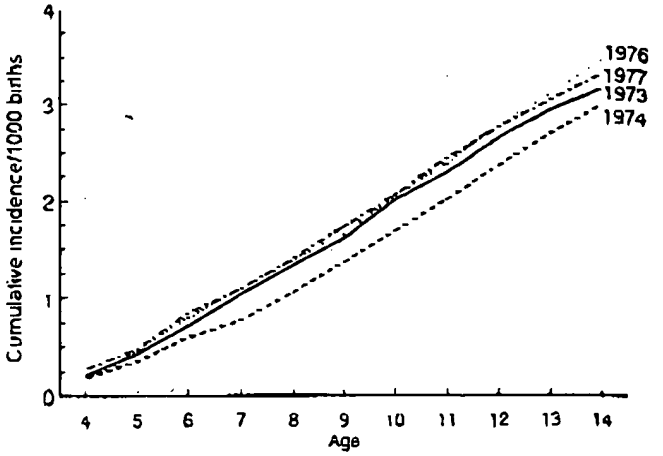

Fig. 1 Cumulative incidence of childhood IDDM in Sweden in children 4–15 years born in 1973 (number of diabetic children = 345/107,582 newborns) 1974 (number of diabetic children 329/108.671 newborns) 1976 (number of diabetic children = 342/97.327 newborns) and 1977 (number of diabetic children 320/95,098 newborns)

References

1 Sadelain MWJ, Qin H, Lanzon J, Singh B (1990) Prevention of type 1 diabetes in NOD mice by adjuvant immunotherapy. Diabetes 39: 583–599

2 Havada M, Kishimoto Y, Makino S (1990) Prevention of overt diabetes and insulitis in NOD mice by a single BCG vaccination. Diabetes Res Clin Pract 8: 85–89

3 Shehadeh N, Calcinaro F, Bradley BJ, Bruchhim J, Vardi P, Lafferty KJ (1994) Effect of adjuvant therapy on development of diabetes in mouse and man. Lancet 343: 706–707

4 Dahlquist G, Blom L, Tuvemo T, Nystrom L, Sandstrom A, Wall S (1989) The Swedish childhood diabetes study – results from a nine-year case register and a one year case-referent study indicating that IDDM is associated with both NIDDM and autoimmune disorders. Diabetologia 32: 2–6

5 Ericson A, Gunnarskog J, Gustavsson D, Kallén B, Malker B (1983) BCG vaccination and child cancer in Sweden. In: Crispen RG (ed) Cancer. Elsevier, Amsterdam, pp 411–417

6 Romanov V, Svensson Å, Hallander HO. The impact of changing BCG coverage on tuberculosis incidence in Swedish-born children between 1969 and 1989. Tubercle and Lung Disease 1992, 73: 150–61

Shared amino acid sequences between glutamic acid decarboxylase 65 and 67 and alpha-2-macroglobulin. A focus for cross-reactive autoantibodies?

Dear Sir,

According to the theory of molecular mimicry as an explanation for the development of autoimmune disease, the existence of identical or very similar amino acid sequences between environmental agents (e.g. viruses) and 'self' antigens leads to the immune system cross-reacting against self antigens, hence triggering autoimmunity [1]. In view of the fact that peptides presented by HLA class II molecules are frequently ubiquitous self proteins, we have suggested that mimicry between these and motifs associated with known autoantigens could also trigger autoimmune reactions [2]. In connection with such considerations, we recently noted that a plasma protein, alpha-2-macroglobulin, contains an amino acid sequence bearing a significant homology to the two forms of glutamic acid decarboxylase (GAD_{65} and GAD_{67}) which are well-defined antigens recognised by autoantibodies in insulin-dependent diabetes mellitus (IDDM) [3]. These sequences are PEVKSK on alpha-2-macroglobulin and PEVKEK and PEVKTK on GAD_{65} and GAD_{67}, respectively. Moreover, the immediately succeeding sequences (AIGYL, GMAAL and GMAAV, respectively) would correspond in the main to conservative substitutions. Alpha-2-macroglobulin is an inhibitor of low molecular weight proteases such as trypsin and plasmin [4] and its levels have been reported to be increased in diabetes [5]. These properties of alpha-2-macroglobulin, coupled with the sequence homology, raises an intriguing question of whether T-helper cells, recognising an epitope of alpha-2-macroglobulin presented by HLA class II molecules may also, under certain conditions, respond to GAD, the autoantigen implicated in the autoimmune destruction of beta cells [6]. As an initial test of this hypothesis, we set out to determine whether sera from patients with IDDM have autoantibodies reacting with alpha-2-macroglobulin. We employed an ELISA system established and optimised using polyclonal rabbit anti-human alpha-2-macroglobulin antiserum. Microtitre plates were coated with 200 ng/ml of purified alpha-2-macroglobulin and reacted with five normal sera and ten sera from patients with high titres of anti-GAD antibodies (126 to 212 arbitrary units [7]) followed by reaction with 1 in 6000 dilution of anti-human IgG conjugated to horseradish peroxidase. The substrate used was *o*-phenylenediamine dihydrochloride dissolved in phosphate-citrate buffer containing sodium perborate and the optical density was read in a microplate reader at 490 nm. We found no specific reactivity of these "high titre" sera with alpha-2-macroglobulin as compared to normal sera. Pre-absorption of two sera with the

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